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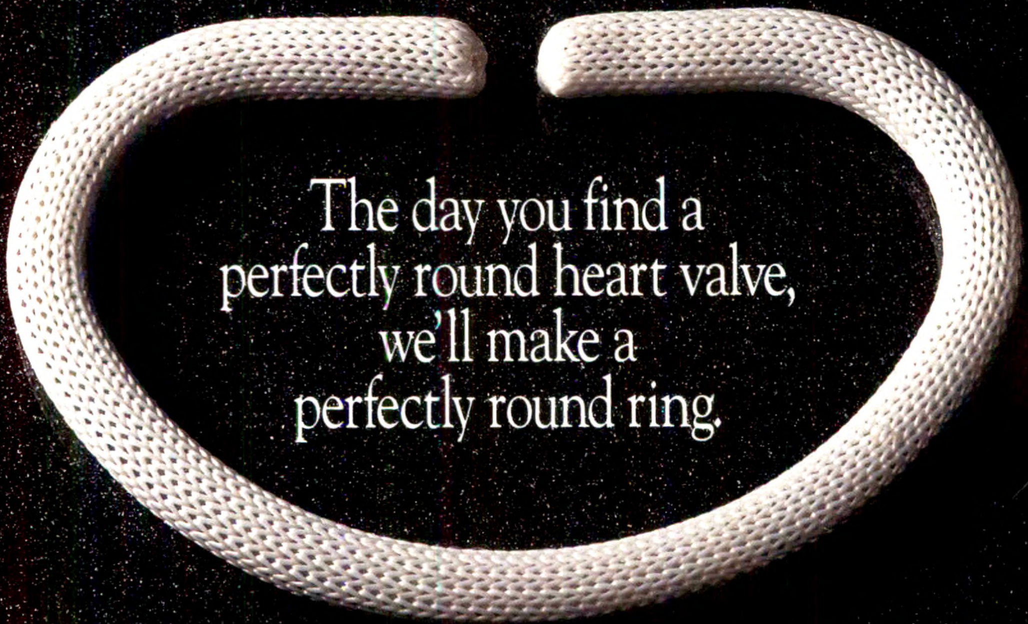

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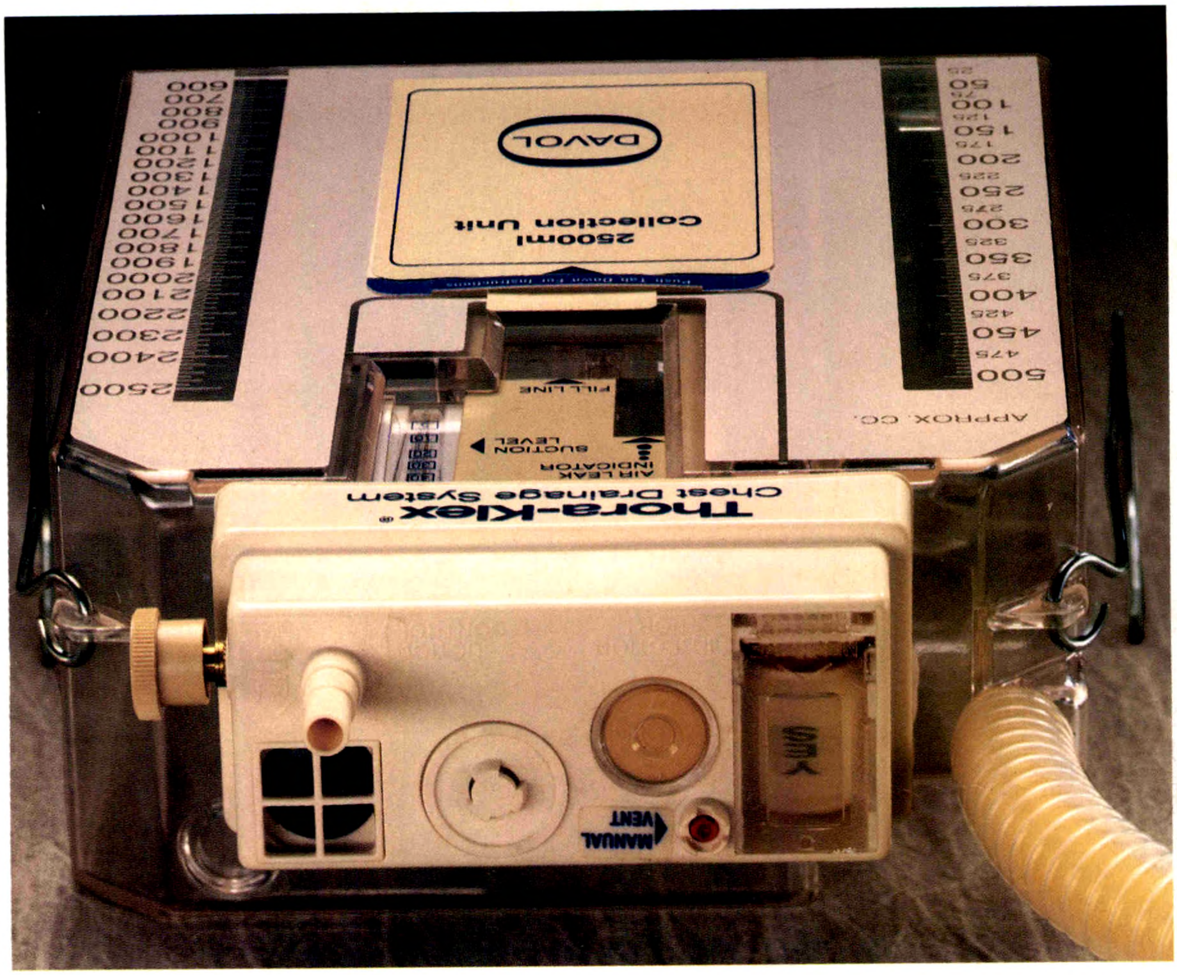

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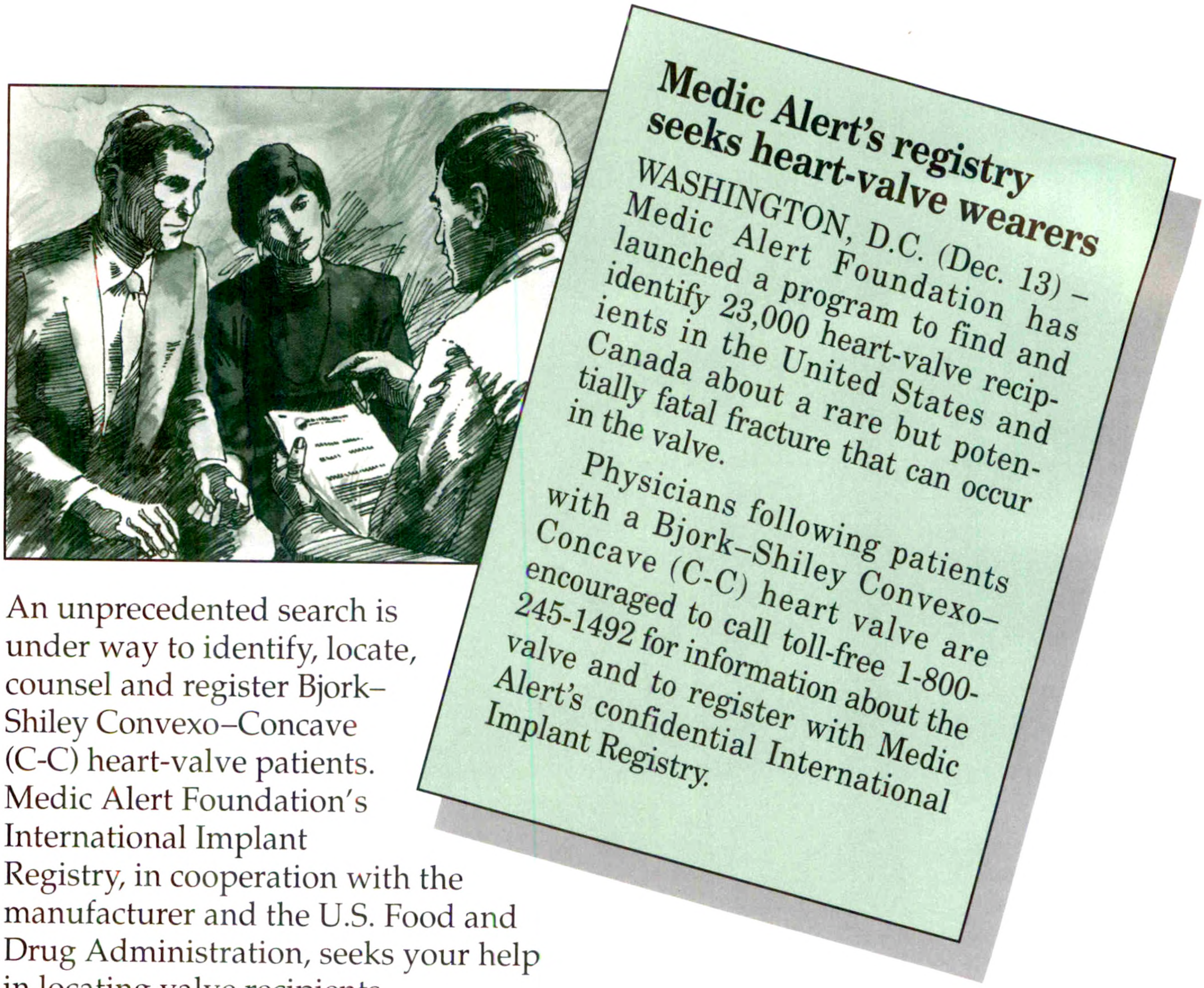

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Volume 51 Number 4

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April 1991

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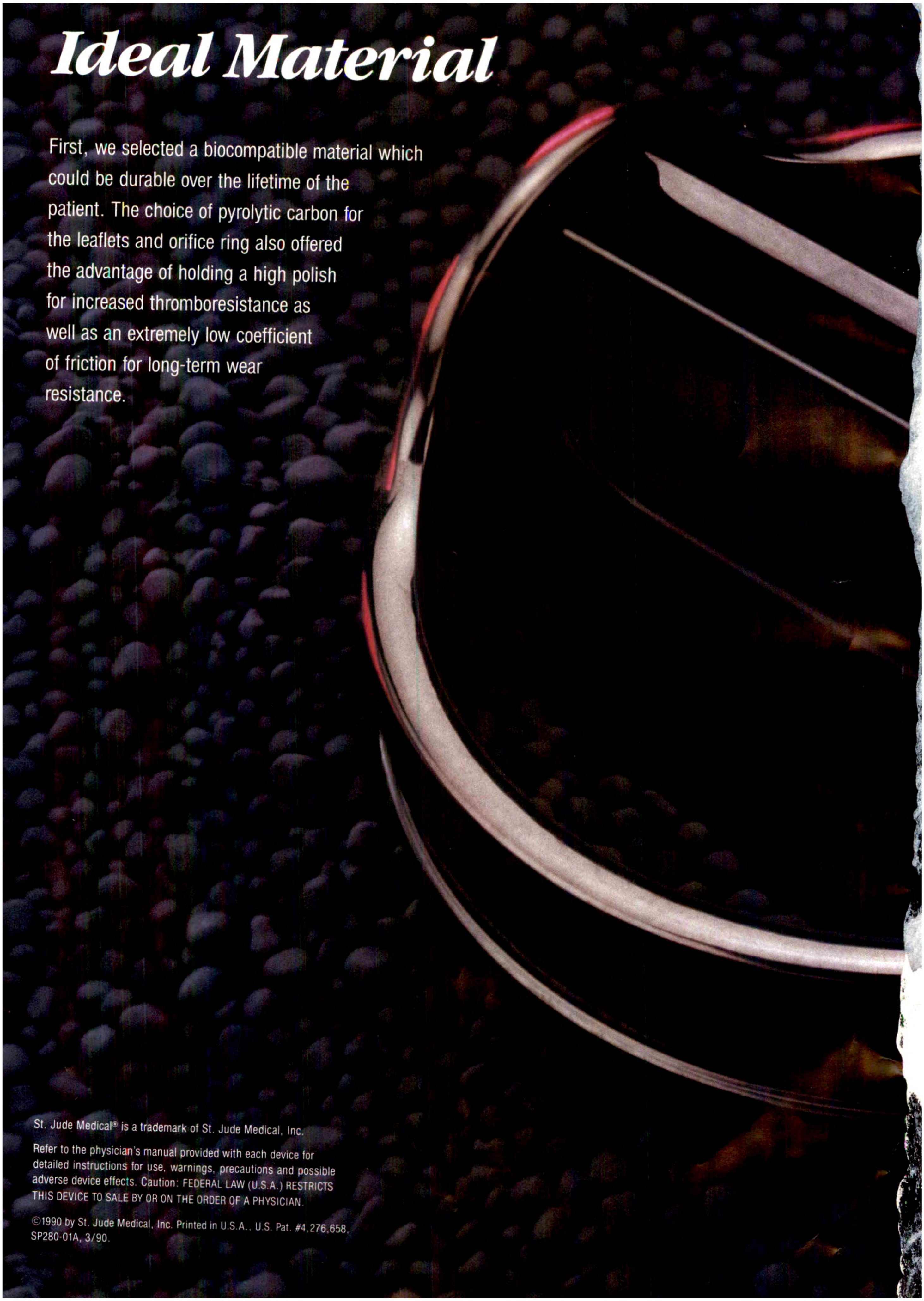

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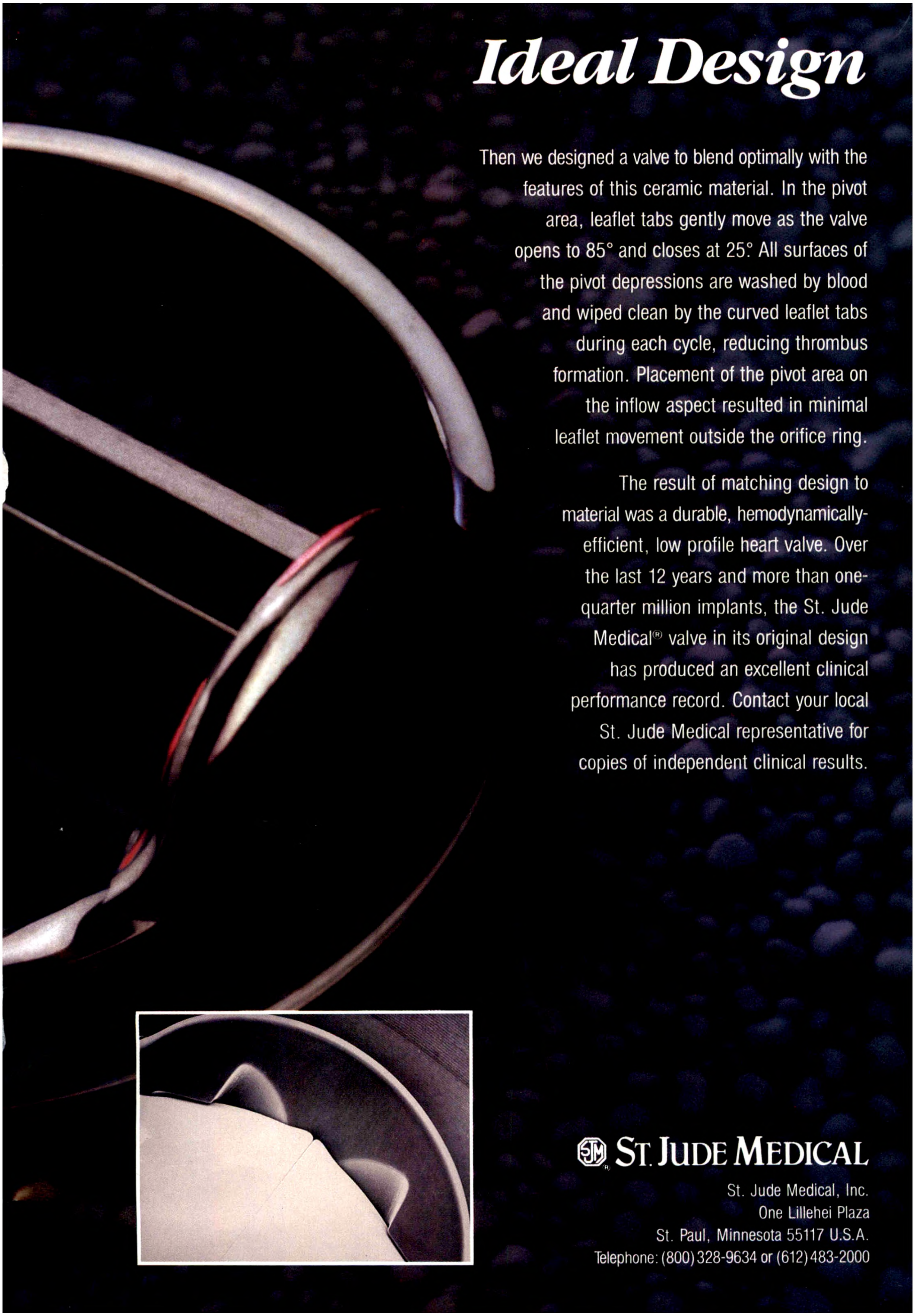

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Indications: Bioprostheses are indicated for use in patients suffering from valvular heart disease. Aortic and mitral valvular heart disease are conditions involving any of the following: obstructions of the heart valves, or stenosis; leakage of the valves, known as regurgitation or insufficiency; and combinations of the two, sometimes referred to as mixed disease or combined lesions. Valvular heart disease may be caused by any number of factors, including congenital abnormalities, infection by various microorganisms, degenerative calcification rheumatic heart disease and rupture or dysfunction of the mitral subvalvular mechanism secondary to myocardial ischemia. Bioprostheses are used particularly in those patients for whom long-term anticoagulation is contraindicated or who may be difficult to maintain on anticoagulation therapy. The Carpentier-Edwards bioprosthesis is intended for use in patients whose aortic or mitral valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic or mitral valve prosthesis which is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. **Warnings:** For Single Patient Use Only In the presence of conditions affecting calcium metabolism or when calcium-containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients under 20 years of age, in patients on a high calcium diet, in the presence of severe systemic hypertension, and in patients who are on maintenance hemodialysis. The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile.** The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions:** 1. When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Carpentier-Edwards bioprostheses to calcification as compared to other commercially available porcine valves. **Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician. Baxter International Inc. is the owner of the following US patent which covers the products described herein: 4,106,129. Patent numbers in foreign countries supplied upon request. See package insert accompanying product for a full discussion of warnings, contraindications, complications and prescribing information. Carpentier-Edwards® is a registered trademark of Baxter International Inc.

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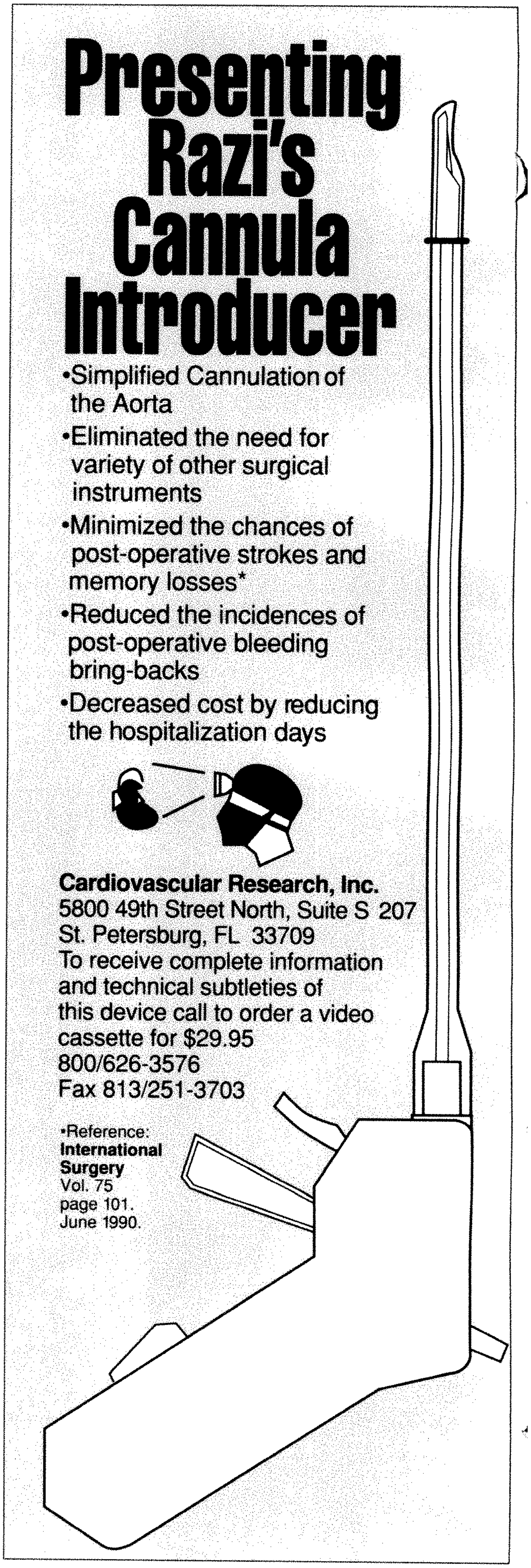

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Second Scientific Meeting of the

International Association for Cardiac Biological Implants

Topic: Infective Endocarditis of Heart Valves

Vista International Hotel - Washington, D.C., U.S.A.
Sunday, May 5, 1991

PROGRAM

PROGRAM FOR THE SECOND SCIENTIFIC MEETING OF THE INTERNATIONAL ASSOCIATION FOR CARDIAC BIOLOGICAL IMPLANTS
(Vista Hotel Ballroom)

5:00 to 8:00pm Saturday, May 4, 1991: Registration

Sunday, May 5, 1991

7:00am Registration

7:00 Continental Breakfast

3:20am: Welcoming Remarks (Dr. S. Gabbay)

First Session - Moderators:
Dr. Bonchek, Dr. Levitsky

3:30 1) **"CHANGING SPECTRUM OF PATHOGENS IN SURGICALLY TREATED ENDOCARDITIS: 1980-1989: MANAGEMENT OF STREPTOCOCCAL AND GRAM NEGATIVE INFECTION."** Windsor Ting, Norman A. Silverman, and Sidney Levitsky.

1:50 2) **"PHYSIOPATHOLOGY OF TRISCUPID VALVULECTOMY WITHOUT REPLACEMENT: TVE."** Agustin Arbulu. Detroit, Michigan.

1:05 3) **"FACTORS INFLUENCING LATE OUTCOME OF ACTIVE NATIVE VALVE INFECTIVE ENDOCARDITIS."** Dieter Horstkotte, Hagen D. Schultz, Wolfgang Bircks, Bovo E. Strauer. Heinrich-Heine University, Dusseldorf.

:20 4) **"PROTHROMBIN TIME (PT) INADEQUATE FOR COUMADIN CONTROL AFTER VALVE REPLACEMENT IN INFECTIVE ENDOCARDITIS."** Dr. Charles R. Spillert, Shlomo Gabbay, and Eric J. Lazaro. University of Medicine and Dentistry, Department of Surgery, Newark, New Jersey.

:35 5) **"THE TEETH AND INFECTIVE ENDOCARDITIS."** Warren G. Guntheroth. University of Washington, Department of Pediatrics, Seattle, Washington.

:50 5) **"MEDICAL TREATMENT OF INFECTIVE ENDOCARDITIS."** Matthew E. Levison. Medical College of Pennsylvania, Philidelphia, PA. (Special Lecture)

0:15 Coffee Break

Second Session - Moderators:
Dr. Frater, Dr. Gott

10:45 (7) **"THE EFFECT OF CARDIOPULMONARY BYPASS ON THE IMMUNE SYSTEM AND SUSCEPTIBILITY TO INFECTION,"** Joe R. Utley, Spartanburg Regional Medical Center, Medical University of South Carolina. (Special Lecture)

11:05 (8) **"RIGHT AND LEFT SIDE INFECTIVE ENDOCARDITIS. CEREBRAL EMBOLI - WHEN TO OPERATE."** Windsor Ting, Norman A. Silverman, and Sidney Levitsky. Robert Wood Johnson University Hospital, New Brunswick, NJ.

11:20 (9) **"INFECTIVE ENDOCARDITIS (IE) IN HUMAN IMMUNODEFICIENCY VIRUS (HIV) CARRIERS: A COMPARISION WITH HIV NEGATIVE POPULATION"** G. Gerosa, C. Danzi, L. Rossi, M. Zanini, C. Muneretto, P. Zardini, D. Casarotto. University of Verona, Italy.

11:30 (10) **"INFECTIVE ENDOCARDITIS IN HIV CARRIER: EARLY POSTOPERATIVE COURSE."** Windor Ting, Norman A. Silverman, Sidney Levitsky. Robert Wood Johnson University Hospital, New Brunswick, NJ.

11:40 (11) **"TEN YEARS OF SURGERY FOR ENDOCARDITIS IN ADDICTS. INFLUENCE OF ADDICTION AND HIV STATUS."** Robert W. Frater, Donato Sisto. Albert Einstien College of Medicine, Bronx, NY.

12:00 Presidential Address and Detication to Dr. Magilligan: Lawrence Bonchek

12:20 Lunch - Monticello Room

1:10 Lunch Lecture: **"LEONARDO DA VINCI'S ANATOMICAL DRAWINGS."** Francis Robicsek, Charlotte, North Carolina.

Third Session - Moderators:
Dr. Gabbay, Dr. Bortolotti

1:45 (12) **"RESULT OF SURGERY FOR ENDOCARDITIS."** R. Bloom, Bernard R., Goldman, G.T. Christakis, T.A. Salerno and the Cardiovascular Surgeons of the University of Toronto, Toronto, Canada.

2:05 (13) **"VALVE REPLACEMENT IN ACTIVE INFECTIVE ENDOCARDITIS."** Dr. Uberto Bortolotti, A. Milano, A. Mazzucco, E. Mossuto, F. Maizza, G. Thiene, V. Gallucci. Departments of Cardiovascular Surgery and Pathology, University of Padova, Italy.

2:15 (14) **"FUNGAL ENDOCARDITIS"** Augustin Arbulu. Detro Michigan.

2:30 (15) **"ALLOGRAFT SURGERY FOR AORTIC VALVE END CARDITIS WITH ROOT ABSCESS."** A.C. Yankah, R. He zer. German Heart Institute, Berlin, Germany.

2:45 (16) **"INFECTIVE ENDOCARDITIS IS A SURGICAL DISEASE** William Roberts, National Institutes of Health, Bethesd MD. (Special Lecture.)

3:00 Coffee Break

Fourth Session - Moderators:
Dr. Cabrol, Dr. Borst

3:30 (17) **"PROSTHETIC AND HOMOGRAFT CONDUIT FOR TREA MENT OF INFECTIVE ANNULO-AORTIC DEHISCENCE.** Joachim Laas, G. Ziemer, H.G. Borst. Hannover Medic School, Hannover, Germany.

3:45 (18) **"SURGICAL TREATMENT OF EXTENSIVE ANNULAR DI STRUCTION IN ACUTE BACTERIAL ENDOCARDITIS"** Arisan Ergin, G. Pogo, J. Galla, S.L. Lansman, M. Estioko, R.B. Griepp. Mount Sinai Medical Center, Ne York, NY.

4:00 (19) **"A COMPARISON OF HOMOGRAFT VERSUS HETER GRAFT FOR AORTIC ENDOCARDITIS."** Patrick J. M guire, William Angell, James H. Oury, Phyllis A. Edward Scripps Clinic & Research Foundation, La Jolla, CA.

4:15 (20) **"SURGERY FOR VALVE ENDOCARDITIS WITH ANNULAR ABSCESS."** Tirone E. David, M.D. Toronto, Ontario Canada.

4:30 (21) **"THE HOMOGRAFT IN AORTIC VALVE ENDOCARDI TIS."** Donald N. Ross. London, U.K.

4:45 Closing remarks: Dr. Hans Borst, Hannover, Germany

5:15 Announcement

Adjournment

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William L. Breckwoldt, MD, Christopher M. Genco, MD, Raymond J. Connolly, PhD, Richard J. Cleveland, MD, and James T. Diehl, MD

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T. Bruce Ferguson, Jr, MD, and James L. Cox, MD

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Amber A. Guth, MD, Thomas H. Gouge, MD, and Harry J. Depan, MD

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Simplified Method for Femoral Venous Cannulation
Michael Rosenbloom, MD, and Alan D. Muskett, MD

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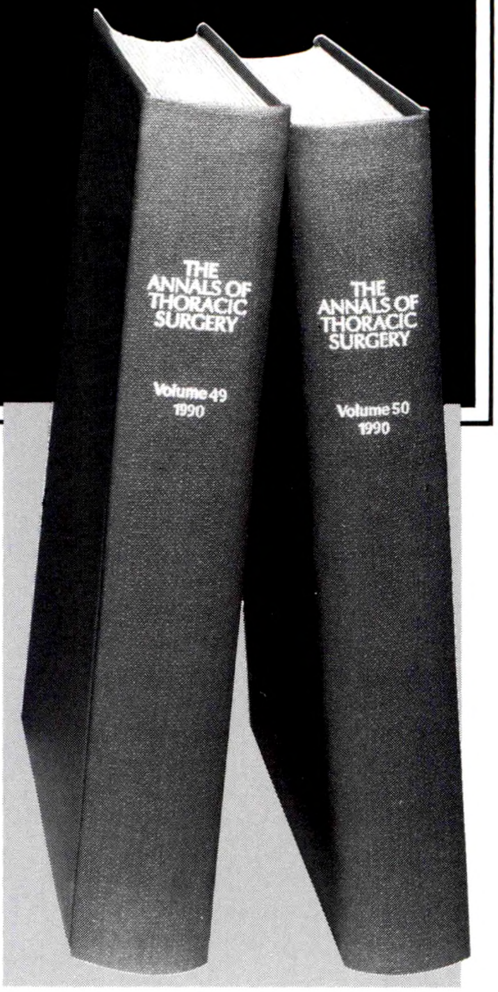
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Epicardial and Endocardial Catheter Ablation for Wolff-Parkinson-White Syndrome

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In this issue, Bockeria and colleagues [1] report catheter ablation with direct-current shock applied epicardially for Wolff-Parkinson-White (WPW) syndrome under heart-lung bypass. They obtained good results—a 98% success rate for the free wall accessory pathway (ACP) and 0.5% mortality in a series of 201 patients—but preferred endocardial operation for septal ACPs. Readers may be dissatisfied, however, that they did not describe in greater detail the patient spectrum and results, which makes it difficult to evaluate properly the true value of this procedure as compared with other surgical methods.

A large part of this report is devoted to proving that this procedure does not adversely affect the myocardium and cardiac function. However, the necessity for such an extensive study itself makes one suspect the possibility of occurrence of myocardial damage. I assume that this procedure destroys or burns the ACP electrically. There is no reason to suppose that the surrounding myocardium, which is essentially of the same composition as the ACP, is not similarly damaged. The ST changes in the electrocardiogram recognized after the procedure, even for the short period up to 9 days, obviously indicate some myocardial damage due to the procedure. The support of heart-lung bypass was needed for this simple procedure, which was probably necessary to protect cardiac function from acute hemodynamic and arrhythmic derangements after discharge of condensed high energy from the catheter electrode tip. Bockeria and associates' enthusiastic epicardial use of catheter ablation for WPW syndrome, however, will be less attractive now to cardiologists, because another catheter ablation method achieved by the intravenous and intraarterial routes without the necessity of opening the chest is becoming practical. On the other hand, the work of Bockeria and associates provides some important information as well as a warning about the method of endocardial catheter ablation.

See also page 563.

Fischer and co-workers [2] proposed catheter ablation with direct-current shock in 1982. The catheter electrode was inserted into the coronary sinus through a vein. Subsequently, this method was tried by many other investigators, but has been almost completely abandoned because of the many associated complications such as rupture and thromboembolism of the sinus as well as a low rate of success.

Instead, Warin and colleagues [3, 4] recently reported good results with catheter ablation of ACPs in every location. In their series of 70 consecutive patients, preexcitation disappeared in 63 patients, with no recurrence of arrhythmia in 68 patients. Serious side effects were limited to complete atrioventricular block in 2 patients. Warin and colleagues' reports encouraged some invasive cardiologists to treat WPW syndrome patients nonpharmacologically by themselves. We believe, however, that the real value of catheter ablation first requires careful and exhaustive evaluation.

First, the spectrum of Warin and colleagues' [3] patients was quite different from that of our surgical patients. Our series was very similar to other large series surgically treated by Gallagher [5], Cox [6], and their associates. The age range of Warin's 35 consecutive patients was 14 to 65 years. The age range of our 424 consecutive surgical patients (December 1990) was 5 months to 74 years including 21 (or 5.0%) less than 10 years and 26 (or 6.1%) older than 60 years. Warin's series did not include children and included only 2 relatively elderly patients, aged 64 and 65 years, respectively. The hearts of small children are too tiny to receive the three or four catheters required for catheter ablation. The friable hearts of small children and elderly persons are subject to catastrophic hemodynamic and arrhythmic derangements immediately after discharge of direct-current shock, and even rupture may occur. Bockeria and associates [1] supported the heart by heart-lung bypass in all cases during open chest catheter ablation. It is well known that discharge of endocardial direct-current shock causes considerable burning of the endocardium, barotrauma, incessant tachyarrhythmia, and even ventricular fibrillation in many occasions [7]. The same derangements are likely to occur when performing catheter ablation for WPW syndrome. The outcome of such myocardial damage is not yet clarified. I am afraid, however, that late sudden death after catheter ablation, as has been reported by Evans and associates [8], may be related to this myocardial damage.

Warin and colleagues' [3] series included only 8 patients with left-cardiac–type ACPs, with the remaining 27 patients having the right cardiac type. Large series of surgical cases [5, 6, 9] have always shown that the distribution of ACPs is about even in the right and left heart, or slightly more frequent in the left heart. The reason for this imbalance in Warin's series is obvious; namely, they excluded patients without a patent foramen ovale, because they could not insert the catheter in the left heart as they stated. It is well known that a patent foramen ovale is found in approximately 20% of the normal population.

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In other words, four times as many left cardiac cases were excluded as were included in this series, and should thus be counted as technical failures of the procedure, or the authors should not use the word "consecutive" to characterize their series. In short, their cases consisted of only highly selected and favorable cases for catheter ablation.

Furthermore, the presentation and method of evaluating results of Warin and colleagues are very different from those used by us surgeons. They did not describe the procedures used to ablate the multiple ACPs. Did they fulgurate multiple ACPs at the different sites, which is the routine surgical practice? Probably they did not, because (1) the electrical energy they used for multiple ACPs did not exceed that used for the single ACP cases, (2) they indicated that 2 of the 4 patients with multiple ACPs studied electrophysiologically after operation showed retrograde conduction. These cases should be considered as treatment failures, although they were assigned to the group of successful cure. Most of our own unsuccessful cases so described were those in which one of the multiple ACPs remained but was concealed, with tachycardia not recurring [9–11].

Our series included 55 patients (or 12.9%) with combined congenital and 31 (or 7.3%) with acquired cardiac diseases, most of which were operated on at the same time as the ACP ablation under heart-lung bypass. All of the 11 deaths in the 424 operated patients occurred in this combined cardiac disease group, whereas none of the patients with WPW syndrome alone have died during the past 20 years. In the most recent 160 consecutive patients including 23 patients with combined cardiac disease receiving simultaneous operation, we achieved success rates of almost 100%, ie, no recurrence, no reoperation, no atrioventricular block, and no death, although one of multiple ACPs remained in 2 patients without tachycardia [10, 11].

Some groups have reported extremely good results with catheter ablation, whereas Evans and associates [8] recently reported 65 patients receiving catheter ablation of ACPs in international multicenter studies at the annual meeting of the American Heart Association in November 1990. Of these 65 patients, 3 patients died, including 1 procedure-related and 2 sudden deaths. Accessory pathway operation was required in 17 patients after failed catheter ablation. Major complications occurred in 13 patients and were fatal in 1. The catheter ablation was effective in 57% including 8% (or 5 patients) who still required drug therapy after the procedure.

We know that the approach to left ACPs is much improved by retrograde arterial insertion of the catheter, and that use of radiofrequency waves is much less traumatic. Even so, results of catheter ablation are far worse than those of operation if the results of all kinds of WPW syndrome are compared. Nevertheless, catheter ablation is likely to be even more widely used in the future for the simple reason that patient acceptance will be high. The future situation of treatment of WPW syndrome will probably be very similar to the situation that exists at present regarding percutaneous transluminary coronary angioplasty versus aortocoronary bypass grafting in the management of ischemic heart disease. But, investigators proposing a new method of treatment and comparing it with an already established method must report their results in a thorough, fair, and critical manner. Also, the new method proposed should be easy to perform by an average doctor in the field. Evans and associates' report taught us, however, that catheter ablation is still in the process of development and is a difficult procedure to perform in average cardiac centers. I am concerned that if the present enthusiasm among invasive cardiologists for catheter ablation for WPW syndrome leads to its widespread application in many cardiac centers throughout the world, there will be many failures, complications, and even deaths in an era when already well-established surgical methods are achieving an almost 100% success rate in all forms of WPW syndrome.

References

1. Bockeria LA, Kupatadze NI, Saprigin DB, et al. Surgical treatment of the Wolff-Parkinson-White syndrome by epicardial electrical ablation. Ann Thorac Surg 1991;51:563–72.
2. Fisher JD, Brodman R, Kim SG, Matos JA. Nonsurgical Kent bundle ablation via the coronary sinus in patients with the Wolff-Parkinson-White syndrome [Abstract]. Circulation 1982;66(Suppl 2):375.
3. Warin JF, Haissaguerre M, Lemetayer P, Guillem JP, Blanchot P. Catheter ablation of accessory pathways with a direct approach. Results in 35 patients. Circulation 1988;78:800–15.
4. Warin JF, Haissaguerre M. Fulguration of accessory pathways in any location: report of seventy cases. PACE 1989; 12(Part 2):215–8.
5. Gallagher JJ, Selle JG, Svenson RH, et al. Surgical treatment of arrhythmias. Am J Cardiol 1988;61:27A–44A.
6. Cox JL, Gallagher JJ, Cain ME. Experience with 118 consecutive patients undergoing surgery for the Wolff-Parkinson-White syndrome. J Thorac Cardiovasc Surg 1985;90:490–501.
7. Fontaine G, Scheinman MM. Ablation in cardiac arrhythmias. Mount Kisco: Futura, 1987.
8. Evans GT Jr, Huang WH, CAR investigators. Catheter ablation of accessory atrioventricular pathways: early results of a prospective international multicenter study [Abstract]. Circulation 1990;82(Suppl 3):690.
9. Iwa T, Mukai K, Misaki T, Mitsui T, Matsunaga Y. Surgical management of the Wolff-Parkinson-White syndrome. In: Iwa T, Fontaine G, eds. Cardiac arrhythmias. Recent progress in investigation and management. Amsterdam: Elsevier Science Publishers B.V., 1988:239–50.
10. Iwa T, Misaki T, Tsubota M, Ishida K. Surgical management of tachyarrhythmias. Am J Cardiol 1989;64:87J–91J.
11. Iwa T, Misaki T, Tsubota M, Watanabe G. Direct surgery for tachycardias. In: D'Alessandro LC, ed. Heart surgery 1989. Rome: Casa Editrice Scientifical Internationale, 1990:543–60.

Prospects for Understanding and Eliminating the Deleterious Effects of Cardiopulmonary Bypass

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The article in this issue by Gu and colleagues [1] on the protective effects of the membrane oxygenator on pulmonary injury during cardiopulmonary bypass (CPB) represents another important piece of the complex puzzle relating CPB to its deleterious effects on organ function. For many cardiac surgeons there may be skepticism about the importance, the magnitude, or even the existence of these so-called damaging effects of CPB. Clearly, in the most common cardiac surgical arena of acquired heart disease in the adult patient, the anticipated hospital mortality for patients in the first seven decades of life suffering from acquired mitral valve disease, aortic valve disease, or coronary artery disease who undergo cardiac operations is generally less than 3%. Most patients convalesce normally with little evidence of morbidity.

The Phenomenon

Despite the normal convalescence of the vast majority of patients undergoing open cardiac operations, the experienced surgeon will occasionally see the patient who has an adverse reaction to the CPB experience (the "postperfusion syndrome"), with evidence of prolonged pulmonary insufficiency, excessive accumulation of extravascular water, and to a variable degree, renal and other organ dysfunction, hyperthermia, vasoconstriction, and coagulopathy. These sequelae of CPB may occur in the face of an apparently effective and complete cardiac operation with good hemodynamic performance. Such occurrences are more frequent if the surgeon operates on infants and neonates or the very elderly.

See also page 573.

Dating from the early experience with open heart surgery, surgeons have noted the tendency for extravascular fluid accumulation in patients after CPB. Cleland and colleagues at the Mayo Clinic [2] published their observations in 1966 and related the increase in extravascular fluid to the duration of CPB. It was not until 1987, however, that Smith and colleagues [3] provided the first direct evidence for increased microvascular permeability after CPB using ultrafiltration techniques in a canine model. Using the microvascular colloid osmotic sieving ratio determined by minimal lymph-plasma protein ratios, these investigators demonstrated an increase in permeability to proteins after 2 hours of normothermic CPB in the dog.

Possible Mechanism

It has been hypothesized that the damaging effects of CPB are related to the exposure of blood to abnormal surfaces and conditions, which then initiates a systemic inflammatory response involving both formed and unformed blood elements that normally act locally at sites of injury [4]. A critical aspect of this "whole body inflammatory response" involves the humoral amplification system, which includes the coagulation cascade, the kallikrein system, the fibrinolytic system, and the complement cascade. The damaging effects of CPB likely result in large part from the activation and interaction of these cascades.

The organ most commonly associated with CPB-induced dysfunction is the lung. During the initial phase of CPB, complement is activated primarily through the alternative pathway [5], resulting in release of the anaphylatoxins C3a and C5a. Increased pulmonary and other subsystem morbidity has been associated with higher complement C3a levels during CPB [6]. Chenoweth and Hugli [7] demonstrated specific binding sites on neutrophils for the anaphylatoxin C5a. After cleavage of C5 in the complement cascade another active component, pore-forming C5b-9 complex, is known to stimulate arachidonic metabolism and further promote granulocyte activation [8]. Salama and colleagues [8] have demonstrated pore-forming C5b-9 complexes on neutrophils as well as on erythrocytes during CPB. The end result is leukocyte activation and subsequent deposition in the lungs and other organs. Transpulmonary leukocyte sequestration occurs during partial bypass [5], and previous studies in patients on hemodialysis demonstrated transient neutropenia with temporary pulmonary dysfunction associated with complement activation at the beginning of hemodialysis [9, 10]. In a sheep model, Flick and colleagues [11] showed that leukocytes are required for the increased pulmonary water seen after microembolization. These effects of CPB may in part result from oxygen free radical release [1] during pulmonary reperfusion and lysosomal enzyme release from activated neutrophils [12, 13]. It thus appears that leukocyte (and possibly platelet) activation and sequestration are closely linked to the changes in extrapulmonary water and to occasional pulmonary dysfunction observed after CPB.

Over the past several years, the literature has been replete with studies demonstrating high circulating levels of metabolic by-products of the various cascades as well as other inflammatory by-products during CPB. Unfortunately, the vast majority of these studies simply identify

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the presence of various inflammatory by-products or mediators without showing some relevance to patient morbidity after CPB. Because most patients tolerate the experience of CPB extremely well, there must be a sophisticated natural process that allows neutralization, inhibition, or interruption of these pathways and the prevention of important organ damage in most patients.

Who Is at Risk?

Identification of specific patients at greatest risk for these adverse effects has proved difficult. It does appear that small neonates and infants readily manifest accumulation of extravascular water, and very elderly patients, particularly with preexisting pulmonary disease, seem especially susceptible to pulmonary dysfunction after CPB. It also appears that the duration and extent of damage is ameliorated in the presence of robust cardiac performance. Unfortunately, little progress has been made in identifying specific patient subsets who are at greatest risk for suffering serious morbidity or mortality from this syndrome. It is also of interest that the occasional severe reaction to protamine administration after CPB may relate to activation of the classic complement pathway by the protamine-complement complex [14, 15]. Little is known about the factors that make some patients more susceptible to this reaction.

Methods of Attenuation

The complexity of intervening to attenuate or eliminate these damaging effects relates undoubtedly to the myriad of ways in which these inflammatory (or immunologic) systems can be activated and interact one with another. Methods of attenuating the adverse response to CPB have focused largely on oxygenator components. The nylon-mesh liner in some bubble oxygenators has been found to activate complement [5], and several oxygenator companies have replaced the nylon mesh with polyester or polypropylene. More recently, the membrane oxygenator has demonstrated some advantages with respect to complement activation and transpulmonary leukocyte sequestration. Tamiya and colleagues [16] noted greater complement anaphylatoxin C3a and C5a production in bubble than membrane oxygenators. Gu and colleagues [1] demonstrated increased platelet and leukocyte deposition in the lungs with the bubble oxygenator as compared with the membrane. Cavarocchi and colleagues [17] observed these phenomena, but the differences between membrane and bubble oxygenators were eliminated when methylprednisolone (30 mg/kg) was administered before CPB with a bubble oxygenator.

To date, however, few specific agents have been identified or tested that block the components of the humoral amplification system or the likely final common pathways for these damaging effects in humans. Aprotinin inhibits plasmin and kallikrein [18, 19] and is useful clinically to decrease bleeding after CPB [20]. Specific blocking agents or antibodies for the kallikrein, fibrinolytic, and/or complement systems will undoubtedly eventually be available clinically, but there is considerable doubt regarding the ability to prevent the inflammatory response to CPB by blocking just one or two of the inflammatory cascades, particularly because there appear to be multiple avenues available to elicit the inflammatory response. A more promising approach might be to identify and block the final common pathway that is responsible for a large component of the clinically apparent adverse effects of CPB. Although platelets and other vasoactive substances may be important, increasing interest has focused on the neutrophil as possibly the key component in this process. In the coming years, it may be possible to transiently (for 24 to 48 hours) inactivate neutrophils or prevent their adherence to endothelial surfaces by monoclonal antibodies or other substances, thereby preventing their sequestration (and subsequent deleterious effects) in the lungs and other organs.

Eventually, the results of most complex cardiac surgical operations will hopefully depend solely on the surgeon's wisdom and expertise in attaining an accurate and complete repair. Currently, two major obstacles thwart the reproducible attainment of that goal: our inability to reproducibly attain complete myocardial protection and the occasional damaging effects of CPB. I suspect that within the next 10 years we will approach the elimination of these obstacles.

References

1. Gu YJ, Wang YS, Chiang BY, Gao XD, Ye CX, Wildevuur CRH. Membrane oxygenator prevents lung reperfusion injury in canine cardiopulmonary bypass. Ann Thorac Surg 1991;51:573–8.
2. Cleland J, Pluth JR, Tauxe WN, Kirklin JW. Blood volume and body fluid compartment changes soon after closed and open intracardiac surgery. J Thorac Cardiovasc Surg 1966;52: 698–705.
3. Smith EEJ, Naftel DC, Blackstone EH, Kirklin JW. Microvascular permeability after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1987;94:225–33.
4. Kirklin JK. The postperfusion syndrome: inflammation and the damaging effects of cardiopulmonary bypass. In: John Tinker, ed. Cardiopulmonary bypass current concepts and controversies. Monograph. Philadelphia: W.B. Saunders, 1989:131–46.
5. Chenoweth DE, Cooper SW, Hugley TE, et al. Complement activation during cardiopulmonary bypass: evidence for generation of C3a and C5a anaphylatoxins. N Engl J Med 1981;304:497–503.
6. Kirklin JK, Westaby S, Blackson EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86: 845–57.
7. Chenoweth DE, Hugli TE. Demonstration of specific C5a receptor on intact human polymorphonuclear leukocytes. Proc Natl Acad Sci USA 1978;75:3943–7.
8. Salama A, Hugo F, Heinrich D, et al. Deposition of terminal C5b-9 complement complexes on erythrocytes and leukocytes during cardiopulmonary bypass. N Engl J Med 1988; 318:408–13.
9. Craddock PR, Fehr J, Brigham KL, et al. Complement and

leukocyte-mediated pulmonary dysfunction in hemodialysis. N Engl J Med 1977;296:769–74.
10. Craddock PR, Fehr J, Dalmasso AP, et al. Pulmonary vascular leukostasis resulting from complement activation by dialyzer cellophane membranes. J Clin Invest 1977;59:879–88.
11. Flick MR, Perel A, Staub NC. Leukocytes are required for increased lung microvascular permeability after microembolization in sheep. Circ Res 1981;48:344.
12. Rinaldo JE, Rodgers R. Adult respiratory distress syndrome: changing concepts of lung injury and repair. N Engl J Med 1982;396:900–9.
13. Hammerschmidt DE, Stroncek DF, Bowers TK, et al. Complement activation and neutropenia during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1981;81:370–7.
14. Kirklin JK, Chenoweth DE, Naftel DC, et al. Effects of protamine administration after cardiopulmonary bypass on complement, blood elements, and the hemodynamic state. Ann Thorac Surg 1986;41:193–9.
15. Cavarocchi NC, Schaff HV, Orszulak TA, Hamburger HA, Schnell WA Jr, Pluth JR. Evidence for complement activation by protamine–heparin interaction after cardiopulmonary bypass. Surgery 1985;98:525–30.
16. Tamiya T, Yamasaki M, Maeo Y, et al. Complement activation in cardiopulmonary bypass, with special reference to anaphylatoxin production in membrane and bubble oxygenators. Ann Thorac Surg 1988;46:47–57.
17. Cavarocchi NC, Pluth JR, Schaff HV, et al. Complement activation during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1986;91:252–8.
18. Sunamori M, Innami R, Amano J. Role of protease inhibition in myocardial preservation in prolonged hypothermic cardioplegia followed by reperfusion. J Thorac Cardiovasc Surg 1988;96:314–20.
19. Wiman B. On the reaction of plasmin or plasmin-streptokinase complex with aprotinin or α_2-antiplasmin. Thromb Res 1980;17:143–52.
20. Alajmo FR, Giancarlo C, Perna AM, et al. High-dose aprotinin: hemostatic effects in open heart operations. Ann Thorac Surg 1989;48:536–9.

Cardiopulmonary Perfusion and Cerebral Blood Flow in Bilateral Carotid Disease

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Cerebral infarction is an unexpected and often devastating complication of coronary artery bypass grafting occurring in approximately 2% of patients. Obstructive carotid artery disease is one of the multiple risk factors for perioperative stroke in these patients as outlined in the article by Johnsson and collaborators in this issue [1]. The association between high-grade carotid occlusive disease and stroke after coronary artery bypass grafting has been well documented in several large studies [2, 3]. The mechanism of cerebral infarction in patients with carotid disease undergoing cardiac operations is not well established, but both embolic and watershed (low flow) strokes can occur. Conceivably, the hemodynamic changes associated with cardiopulmonary bypass could cause embolization of thrombotic debris from ulcerated stenotic carotid plaques. Alternately, a stenotic carotid lesion may produce cerebral hypoperfusion during the low systemic perfusion pressures sometimes associated with cardiopulmonary bypass.

The study by Johnsson and co-workers examines this latter possibility of cerebral hypoperfusion during cardiopulmonary bypass. Their observations that cerebral blood flow is not reduced and often increases during cardiopulmonary bypass in patients with evidence of occlusive extracranial cerebrovascular disease are similar to the findings of Gravlee and associates [4]. The carotid disease in the patients reported by Johnsson and associates seemed to be well compensated as evidenced by the nearly identical mean cerebral blood flow before cardiopulmonary bypass in the carotid versus control group. Perioperative stroke did not occur in any of the patients with carotid lesions. However, the studies by Powers and associates [9] referred to in their paper used positron emission tomography in patients with hemodynamically significant unilateral carotid occlusive disease to demonstrate reduced cerebral blood flow or reduced cerebral perfusion pressure in the subset of patients with angiographic evidence of ipsilateral meningeal or ophthalmic artery collateralization. Therefore, cerebral hypoperfusion does occur in some patients with occlusive carotid disease. The risk of perioperative stroke in this subset of patients is unknown. The cerebral hypoperfusion in these patients may be exacerbated by the hemodynamic instability that frequently occurs during cardiopulmonary bypass or perioperatively and leads to cerebral infarction.

See also page 579.

The results of studies on cerebral perfusion, such as this one by Johnsson and co-workers, relate only to the mechanism of stroke. The number of patients in this report is small (7) and therefore does not negate the importance of much larger studies indicating that carotid occlusive disease increases the risk of stroke in patients undergoing coronary artery bypass. Johnsson and associates point out that the degree of carotid stenosis is thought to be the primary determinant for a neurological complication after coronary artery bypass grafting. Similarly, only patients with serious carotid lesions (>80%) are considered to be candidates for a prophylactic carotid endarterectomy. The degree of carotid stenosis (percent) was not stated in this report; hence, it is unknown if these patients would be acceptable candidates for a carotid operation. Indeed, in the 7 patients with carotid disease, 5 of the 14 carotid arteries were occluded. Occluded carotid arteries do not respond favorably to carotid endarterectomy and, in most cases, should not be considered for the operation.

Johnsson and associates question the rationale for carotid-coronary operation in neurologically *asymptomatic* patients. However, their cerebral blood flow data do not distinguish between neurologically symptomatic and asymptomatic patients. Therefore they cannot be used to justify or refute operation in a particular group.

Finally, combined carotid-coronary revascularization is not the only surgical option in managing these patients. Most cardiac and vascular surgeons prefer, when possible, to perform the carotid and coronary revascularization as separate (staged) operations. If the cardiac disease is stable, the carotid procedure can frequently be done before cardiac revascularization under local anesthesia or a carefully administered general anesthetic even in the presence of serious cardiac disease. Patients with high-grade carotid stenosis and unstable coronary artery disease may be managed by a combined carotid-coronary revascularization or coronary artery bypass grafting first followed by a carotid procedure at a later date (reverse stage). Hertzer and collaborators [6] prospectively studied a group of such patients and found a 2.8% incidence of stroke in 71 patients randomized to a combined carotid-coronary procedure. The cumulative incidence of stroke in 58 patients randomized to a reverse-staged procedure was 14% ($p = 0.042$). Mortality rates were similar, 4.2% versus 5.2%, respectively. Thus, the risk of stroke appears less in combined carotid coronary procedures than in reverse-staged operations.

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In summary, the current report by Johnsson and associates indicates that patients with serious bilateral carotid artery disease do not typically have cerebral hypoperfusion during cardiopulmonary bypass. These data, however, cannot be used to diminish the importance of carotid occlusive disease as a risk factor for stroke. Patients with high-grade carotid disease who require coronary artery bypass grafting are at increased risk for perioperative neurological complications. They should undergo a complete cerebrovascular and cardiac evaluation and the selection of a staged, combined, or reverse-staged carotid-coronary procedure should be made on an individual basis to yield the best results.

References

1. Johnsson P, Algotsson L, Ryding E, Ståhl E, Messeter K. Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease. Ann Thorac Surg 1991;51:579–84.
2. Brener BJ, Brief DK, Alpert J, Goldenkranz RJ, Parsonnet V. The risk of stroke in patients with asymptomatic carotid stenosis undergoing cardiac surgery: a follow-up study. J Vasc Surg 1987;5:269–79.
3. Reed GL III, Singer DE, Picard EH, DeSanctis RW. Stroke following coronary-artery bypass surgery. A case-control estimate of the risk from carotid bruits. N Engl J Med 1988;319:1246–50.
4. Gravlee GP, Roy RC, Stump DA, Hudspeth AS, Rogers AT, Prough DS. Regional cerebrovascular reactivity to carbon dioxide during cardiopulmonary bypass in patients with cerebrovascular disease. J Thorac Cardiovasc Surg 1990;99:1022–9.
5. Powers WJ, Press GA, Grubb RL Jr, Gado M, Raichle ME. The effect of hemodynamically significant carotid artery disease on the hemodynamic status of the cerebral circulation. Ann Intern Med 1987;106:27–35.
6. Hertzer NR, Loop FD, Beven EG, O'Hara PJ, Krajewski LP. Surgical staging for simultaneous coronary and carotid disease: a study including prospective randomization. J Vasc Surg 1989;9:455–63.

Prolonged Pumpless Arteriovenous Perfusion for Carbon Dioxide Extraction

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A method of extracorporeal carbon dioxide extraction from the blood using an efficient microporous membrane oxygenator or membrane gas exchanger was evaluated during pumpless arteriovenous perfusions with a view to its application for partial respiratory support. The first study carried out in dogs revealed some increase in cardiac output, cardiac index, and cardiac work, although this increase was less than that normally expected from the added extracorporeal blood flow. In sheep during 3 to 7 days of continuous bypass, there was practically no hemolysis and relatively stable hemoglobin and hematocrit levels, and the platelet counts remained within safe levels. The maximum extracorporeal blood flow tended to decrease from a mean of 1.55 L/min on day 1 to 1.34 L/min on day 3 to 1.28 L/min on day 7. Carbon dioxide extraction remained efficient throughout the perfusion, but there was a minimal decrease from the first day (10.92 mmol/L) to the third day (8.46 mmol/L) at the higher blood carbon dioxide concentrations; it remained stable thereafter at 9.0 mmol/L.

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A simple, relatively safe and efficient method of carbon dioxide extraction from the blood might find a number of uses, especially in patients suffering from chronic respiratory failure associated with obstructive lung disease. Although most techniques of extracorporeal membrane oxygenation have been abandoned in adults, the more recent variation of extracorporeal CO_2 removal, combined with low-frequency positive-pressure ventilation for oxygenation through the lungs [1], has been reported to be more successful for the treatment of acute respiratory distress syndrome [2]. However, this technique remains complicated and expensive. It also requires the use of a pump with its inherent problems and potential dangers even at the lower extracorporeal blood flow rates (ECBFRs) employed. Furthermore, it requires highly qualified and well-trained personnel around the clock for a few days.

In the 1960s the first author evaluated a technique of pumpless arteriovenous perfusion for respiratory assistance [3]. It was abandoned because of inadequate blood oxygenation due to the very low ECBFR of these highly resistant and relatively low-efficiency early membrane oxygenators* [4].

Because CO_2 extraction or dialysis alone does not require a high ECBFR [5], and with the development of the new highly efficient and very low resistance microporous membrane oxygenators or membrane gas exchangers (MGEs), this simple mode of pumpless arteriovenous perfusion has now become a valid alternative. To evaluate the usefulness of the technique we proceeded in two steps. We first did a preliminary study to analyze the hemodynamic effects of this type of bypass in dogs during 6 hours of perfusion. We then proceeded to evaluate the hematological and gas exchange capabilities of these MGEs during continuous perfusions of 3 to 7 days' duration in sheep.

Material and Methods

Fifteen mongrel dogs weighing 26 to 32.5 kg and selected according to the Canadian Regulations on Animal Care were anesthetized by an intravenous injection of sodium pentobarbital (Somnotol; MTC Pharmaceuticals, Hamilton, Ont, Canada) at a dose of 25 mg/kg. Whenever necessary, supplemental anesthesia was given by intravenous administration of ketamine hydrochloride (Ketalar; Parke-Davis, Montréal, Qué, Canada), and all animals were ventilated with a Harvard respirator. The left femoral artery and vein were dissected out and fully mobilized. The right femoral artery and the left internal jugular vein were also isolated, the former for measurement of arterial blood pressure and the latter for Swan-Ganz catheter insertion (Swan-Ganz flow-directed thermodilution catheter; Edwards Laboratories, Anasco, Puerto Rico).

The animals were then fully heparinized (100 IU/kg), the femoral vessels were cannulated with the biggest cannulas that could be inserted, and these vessels were ligated distally. The microporous MGE was primed with heparinized Ringer's lactate (4 IU/mL) and connected to the arterial and venous cannulas. An electromagnetic flowmeter (Gould Statham, Oxnard, CA) was inserted at the outlet of the MGE, and pressure manometers were inserted at the inlet and outlet of the device.

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* Although we prefer the term *membrane gas exchanger* for this device because it reflects better its functions, the term *membrane oxygenator* can also be used because of common usage.

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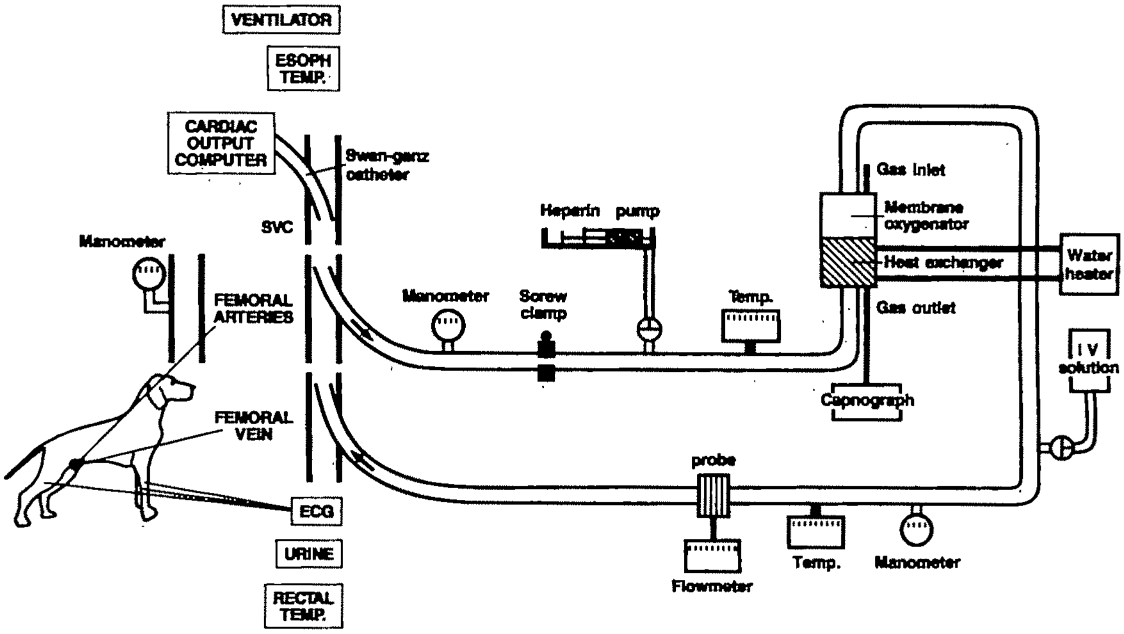

Fig 1. Circuit for pumpless arteriovenous perfusion in dogs. (ECG = *electrocardiogram;* IV = *intravenous;* SVC = *superior vena cava.)*

A screw clamp was placed near the arterial cannulas so that the ECBFR could be adjusted to the desired rate. Temperature probes were also inserted in the rectum and in the MGE (Fig 1). Except for a 60-mL/h drip of normal saline solution, no extra volume was given.

The heat exchanger that is incorporated in these devices was connected to a water heater (Meditherm; Gaymar Industries, Orchard Park, NY), and the temperature of the animal was maintained around 37° ± 0.6°C. During the perfusion, heparin was given to maintain an activated clotting time (hemochron time [Hemochron 400 blood coagulation time; Int Tech Corp, Edison, NJ]) of 400 seconds, and the level of anticoagulation was controlled at hourly intervals.

Hematological studies were carried out before, twice during, and once at the end of the perfusion. Blood was sampled for gas analysis from the mixed venous side of the animal (through the Swan-Ganz catheter), from the inlet (arterial side of the dog), and from the outlet of the gas exchanger. The MGE was ventilated with 100% oxygen at flow rates of 4 L/min, and in one series, it was successively increased to 8 L/min and 12 L/min. The ECBFR was changed gradually by adjusting the screw clamp to obtain flow rates of 200, 400, 600, 800, and 1,000 mL/min. After each change the cardiac output was measured (Cardiac output computer model 9510; Edwards Laboratories, American Hospital Supply Corp, Santa Ana, CA) after a 15-minute period to allow for stabilization. The percentage of CO_2 in the gas leaving the oxygenator was also measured using a Beckman medical gas analyzer (Beckman Model LB-1 medical gas analyzer; Spinco Division, Stanford Industrial Park, Palo Alto, CA). In general, the extraction of CO_2 as measured with the Beckman analyzer was similar to the ones calculated from the blood gases between inlet and outlet of the blood ports of the MGE.

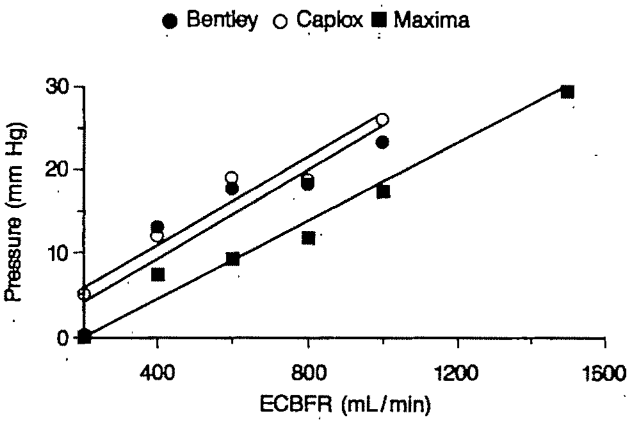

Fig 2. Pressure drop between inlet and outlet in three microporous gas exchangers at various extracorporeal blood flow rates (ECBFRs).

Three series of experiments were carried out in each dog. In the first series, the animals were ventilated with room air to obtain an arterial carbon dioxide tension (Pco_2) of 30 to 40 mm/Hg. In the second series, the CO_2 concentration breathed by the animal was further increased to achieve an arterial Pco_2 of 70 to 80 mm Hg, and in the third series, the arterial Pco_2 was increased to levels varying between 90 and 100 mm Hg.

Cardiac output was measured three times at the various flow rates and Pco_2 concentrations and the average noted. The stroke work and cardiac index were then calculated from these data. Although five commercially available MGEs were studied, only three models (the Bently, the Capiox 11 3.3, and the Maxima) were retained for this analysis. Three dogs were used for the evaluation of each MGE for a total of 9 dogs.

In the second study, 9 sheep averaging 54.8 kg were anesthetized with an intravenous injection of sodium pentobarbital at a dose of 25 mg/kg. Supplemental anesthesia was given as required with intravenous administration of ketamine hydrochloride, and the animals were ventilated with a Harvard respirator. The right carotid artery and jugular vein were dissected out and cannulated with the largest possible cannula and connected to the MGE. The electromagnetic flowmeter was inserted on the outlet of the MGE and the ECBFR was controlled by a screw clamp. A heparinized syringe driven by a Sage pump was connected to the inlet line, and connections for measuring the pressures and temperatures at the inlet and outlet of the oxygenator were available. Heparinization was used to adjust hemochron coagulation time to approximately 400 seconds. These were controlled after adjusting the flow rate in the heparin syringe twice a day.

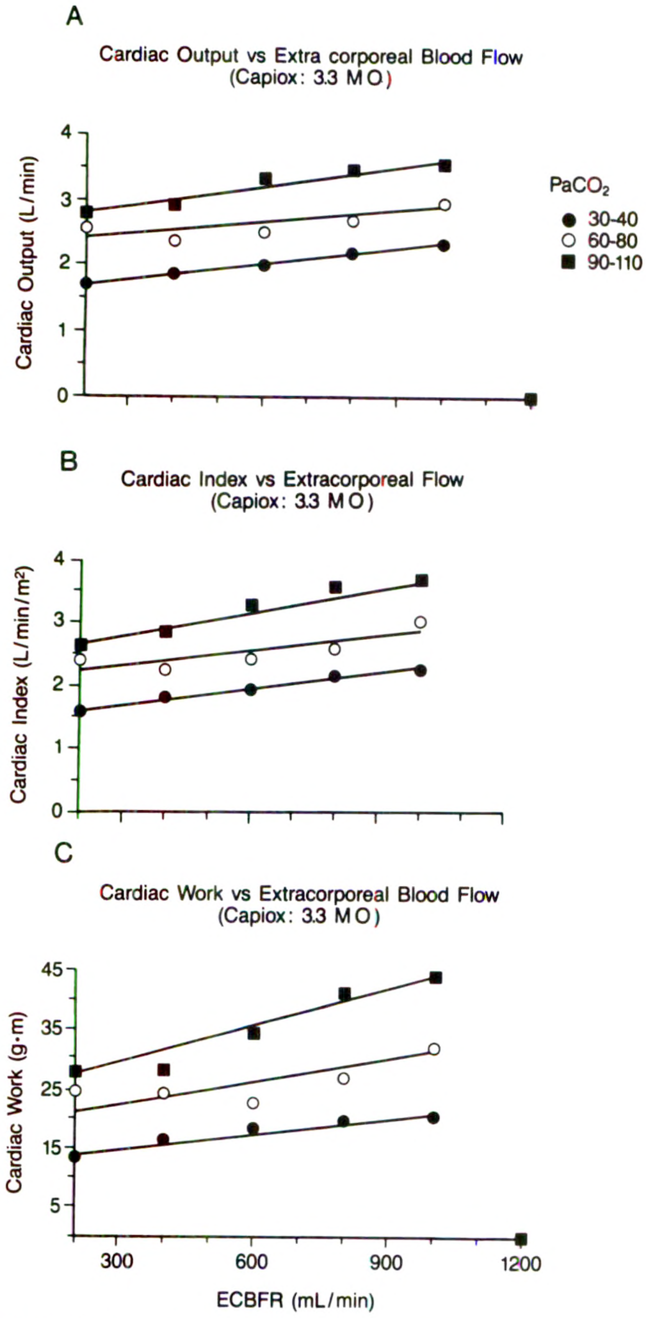

Fig 3. Cardiac output (A), cardiac index (B), and cardiac work (C) at various extracorporeal blood flow rates and at various blood CO_2 concentrations during perfusion in dogs. (ECBFR = extracorporeal blood flow rate; MO = membrane oxygenator; $PaCO_2$ = arterial carbon dioxide tension, in millimeters of mercury.)

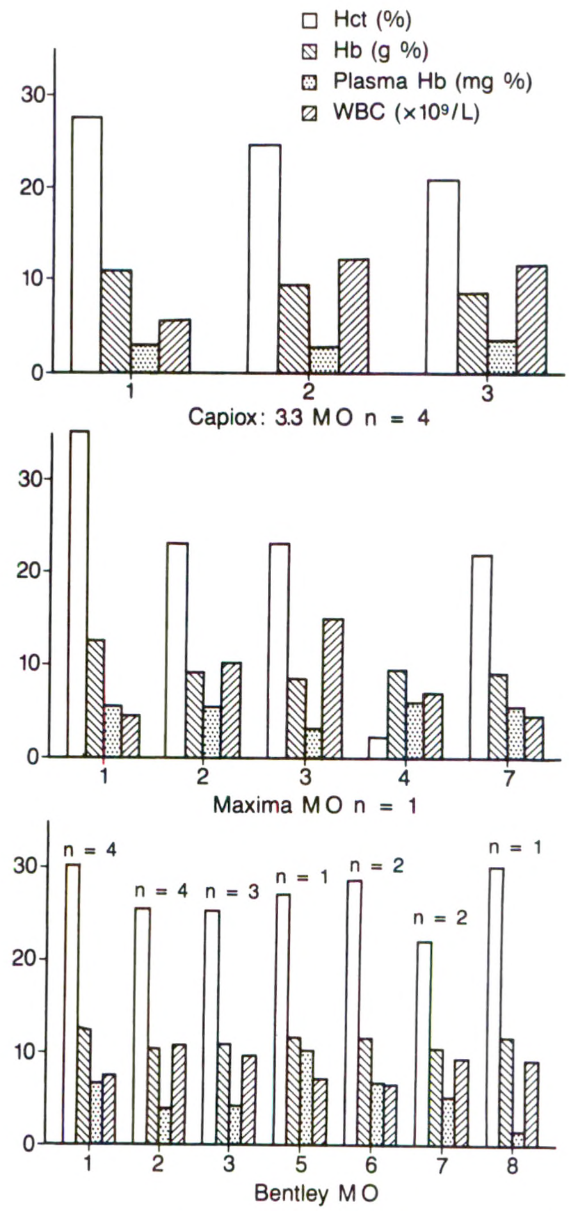

Fig 4. Hemoglobin (Hb) (g%), hematocrit (HCT) (%), plasma Hb (mg%), and white blood cell count (WBC) (×10^9/L) during 3 to 7 days of perfusion in sheep. (MO = membrane oxygenator.)

The animals were then returned to their cage without restraints and fed in a normal fashion. They were brought back daily to the laboratory and, under Valium sedation, made to breathe in a bag connected to an oxygen cylinder so that the arterial Pco_2 could rise gradually. When

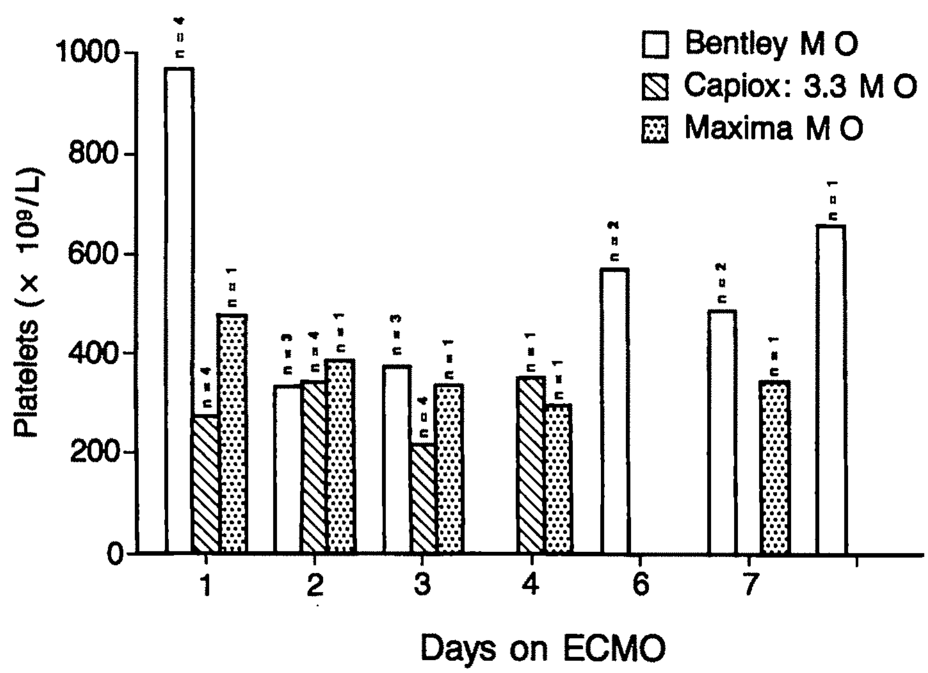

Fig 5. Platelet count during 3 to 7 days of perfusion in sheep. (ECMO = extracorporeal membrane oxygenation; MO = membrane oxygenator.)

necessary, CO_2 was also added to the breathing mixture to attain the arterial CO_2 concentration desired. Blood gases were measured at 15- to 20-minute intervals from the inlet and outlet lines of the MGE. After testing, the animals were then returned to their cages. The experiments lasted from 3 to 7 days, and although ECBFRs greater than 2 L could be obtained with some MGEs, a flow rate averaging 1,300 mL/min was maintained to allow for comparison between the different MGEs. During these experiments the MGEs were ventilated with oxygen at a flow of 8 L/min.

Results

The three MGEs (Bentley, Maxima, and Capiox) chosen for these experiments were very easy to install and simple to prime. They had very low resistance, and the pressure drop between inlet and outlet never exceeded 30 mm Hg up to an ECBFR of 1,600 mL/min (Fig 2). For this reason, blood flow rates of up to 2,300 mL/min could be reached in some of the animals at a normal blood pressure of about 130 mm Hg. In sheep with a blood pressure varying between 110 and 140 mm Hg the mean ECBFR, which on the first day was at 1.55 L/min, tended to decrease slightly to 1.34 L/min on the third day and to 1.28 L/min on the seventh day, mainly because of blood clotting in some of the capillaries of the Capiox and Bentley MGEs.

Hemodynamic analysis carried out in dogs showed an increase in both cardiac output and cardiac index proportional to the increase in ECBFR from 200 to 1,000 mL/min. This increase was, however, less than would have been reflected from the additional ECBFR (Fig 3). An interesting point from this study was that the higher blood CO_2 concentrations produced a corresponding increase in the cardiac output. This was probably because of the vasodilating effect of CO_2.

Blood hemolysis was minor in the three MGEs that were used even after continuous bypass of up to 7 days. The hemoglobin and hematocrit levels tended to decrease immediately after the start of perfusion due to the dilution

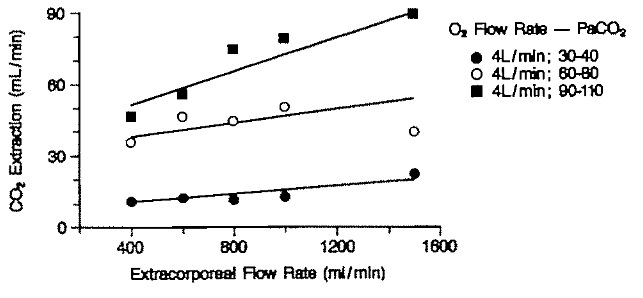

Fig 6. Carbon dioxide extraction from the blood during perfusion in dogs (Maxima membrane gas exchanger). ($PaCO_2$ = arterial carbon dioxide tension, in millimeters of mercury.)

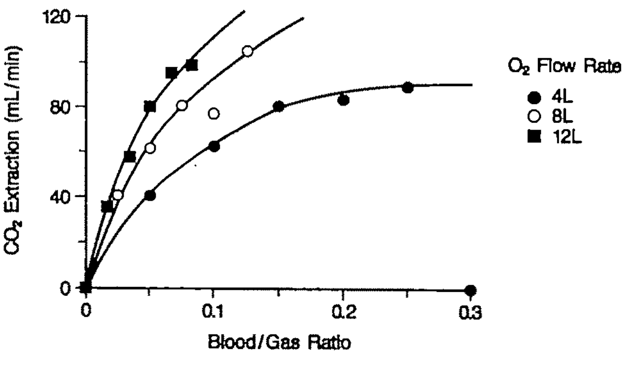

Fig 7. Carbon dioxide extraction at various blood/gas ratios when the Capiox membrane gas exchanger is ventilated with O_2 at flow rates of 4, 8 and 12 L/min. (Arterial carbon dioxide tension ≈ 40 mm Hg.)

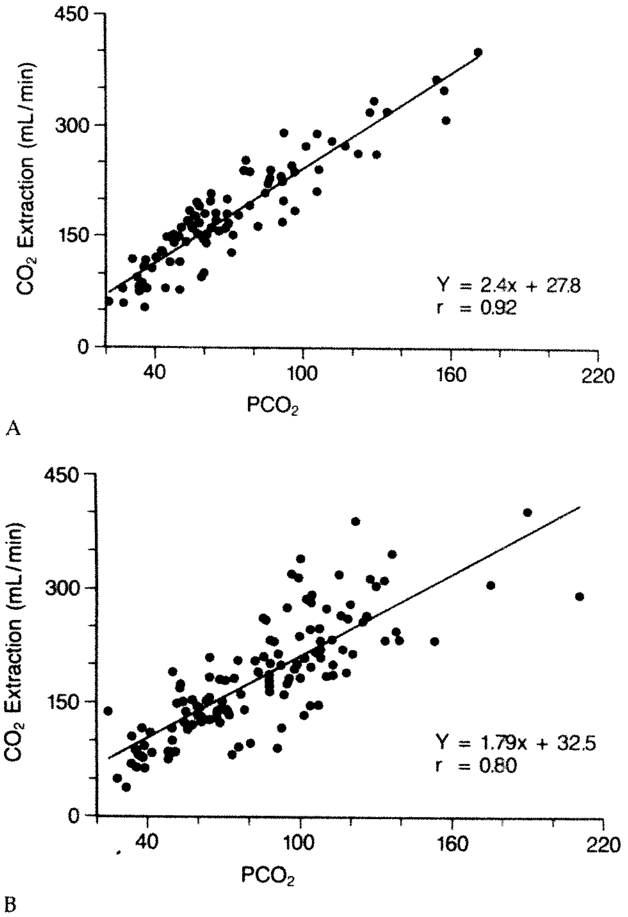

Fig 8. Carbon dioxide extraction at various inlet (arterial) carbon dioxide tensions. (PCO_2, in millimeters of mercury). (A) During 3 days of bypass with the Capiox membrane gas exchanger. (B) During 8 days of perfusion with the Bentley membrane gas exchanger.

from the priming solutions in the MGE. Then, in most animals, it stabilized and even tended to increase slightly except in a few cases where some bleeding occurred (Fig 4). Even after 7 days platelet counts never fell to dangerous levels (Fig 5).

At the lower arterial CO_2 concentrations, the lower ECBFRs were practically as efficient in extracting CO_2 as were the higher flow rates. However, higher ECBFRs were needed for adequate CO_2 extraction when the arterial Pco_2 was increased to more than 60 mm Hg. Extracorporeal blood flow rates of 1,200 mL/min appeared to be adequate up to levels of 100 mm Hg (Fig 6). With the higher arterial Pco_2 and higher ECBFR, increasing the oxygen flow in the MGE from 4 to 8 L/min improved CO_2 removal, but gas flows greater than 8 L/min had little effect on CO_2 elimination (Fig 7). In sheep, carbon dioxide removal from the blood remained very good for the 3 to 7 days of perfusion (Fig 8). Allowing for some variations from day to day, there was only a slight decrease of CO_2 extraction in some of the MGE, likely related to clotting in the capillaries of the device (Fig 9).

Except for 1 animal that was found in the morning bleeding due to a disconnected tube, all animals survived the experiments. The MGEs were also examined at the end of the perfusions, and in one Bentley and two Capiox devices blood was found clotted in some of the capillaries through which the blood flowed. This problem did not exist with the Maxima MGE as the blood flows outside while gases are passed inside the capillaries.

Comment

Pumpless arteriovenous perfusion, although it contributes a certain amount of oxygen to the circulation, is still a relatively inefficient way of saturating the blood. For although ECBFRs of up to 30% of the cardiac output would be sufficient to lower even a high arterial Pco_2 to normal levels such a flow might be insufficient to raise the oxygen saturation to adequate levels if there are very severe pulmonary lesions associated with respiratory failure. Further, this mode of perfusion presents a less efficient configuration, because the blood going to the MGE is already partially saturated and at a higher oxygen tension level than the venous side. These problems are less important when the main goal is CO_2 extraction from the blood [6]. Actually, arteriovenous perfusion for CO_2 removal represents a type of pulmonary dialysis and is more akin to renal hemodialysis than to extracorporeal membrane oxygenation [5, 7]. The studies carried out in dogs show some increase in cardiac output and cardiac work, although this was less than that expected from the additional load of the extracorporeal circulation. Griffith and colleagues [8] have shown that after a period of stabilization and when the ECBFR is maintained at a constant rate not exceeding 35% of the cardiac output, after the initial increase a hemodynamic readjustment eventually occurs. Even in the presence of hypoxia and moderate pulmonary hypertension the cardiac output tends to return to its preperfusion level. This is the result of a proportional increase in the peripheral vascular resistance. In spite of these data, which have been compiled from healthy animals, one should be very careful in using this mode of perfusion in severely ill patients, especially when cardiac abnormalities are present. Still, for patients with relatively good cardiac function it can be useful because the ECBFR can be adjusted to a level that can be tolerated by these patients and efficient for CO_2 extraction. The experiments carried out in sheep have shown that the MGE can be used for CO_2 removal during several days with little or no loss of efficiency and only minor hematological changes.

The simplicity of this technique and its comparative safety in comparison with other methods of extracorporeal membrane oxygenation should encourage its use at an earlier stage of the disease. Further potential advantages would be its cost effectiveness and the possibility of using less specialized personnel. Another advantage is that whenever a problem develops with the MGE such as a leak or loss of effectiveness this can easily be corrected by clamping the two cannulas and replacing the device with a new one. Unless there are intracardiac shunts this mode of perfusion practically eliminates the danger of brain emboli. It also preserves pulse pressure to various

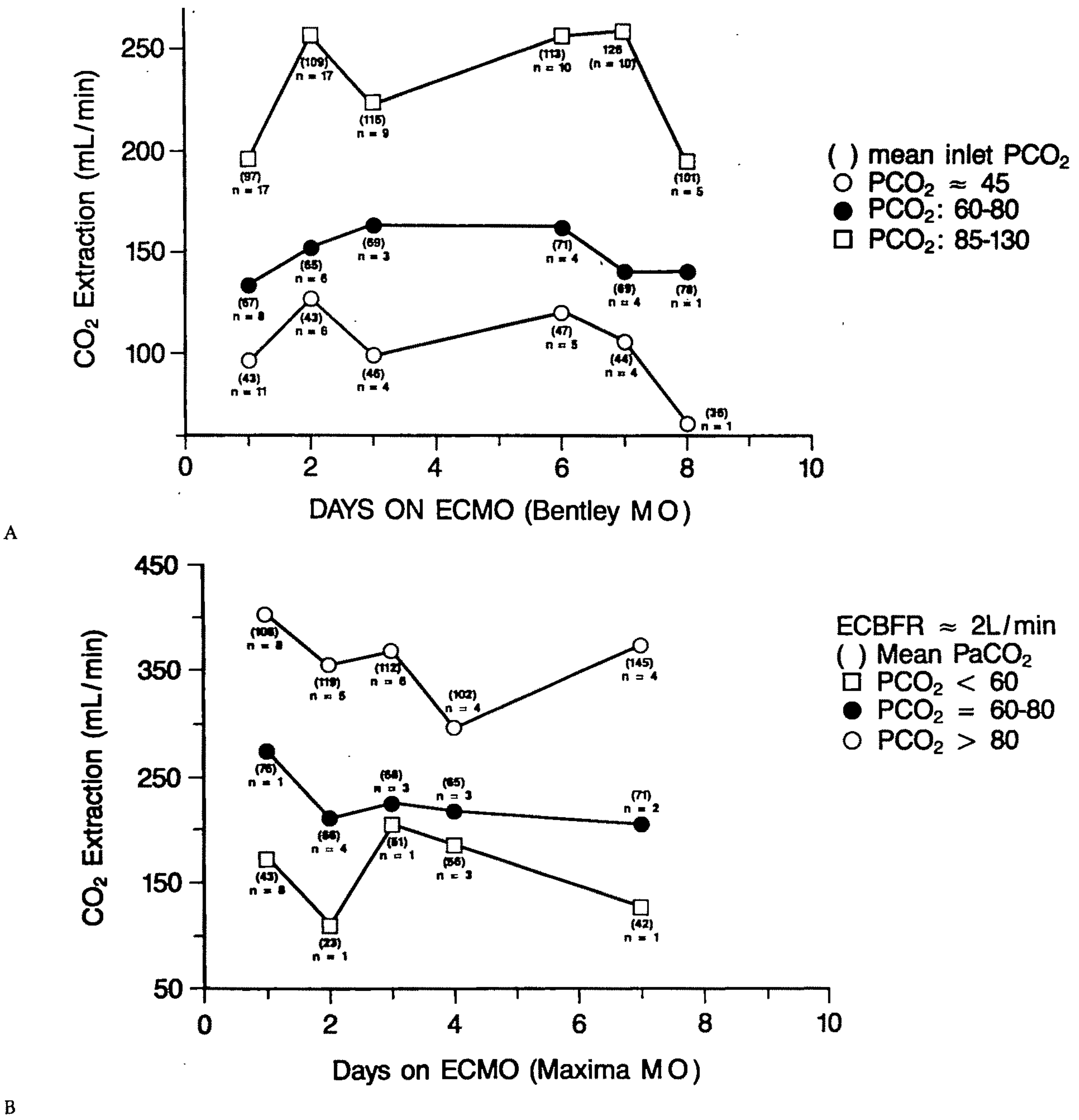

Fig 9. Carbon dioxide extraction at various carbon dioxide tensions (PCO_2, in millimeters of mercury). (A) With the Bentley membrane oxygenator (MO). (B) With the Maxima MO. (ECBFR = extracorporeal blood flow rate; ECMO = extracorporeal membrane oxygenator.)

organs. The oxygenation of pulmonary blood has a vasodilatory effect on the arteriolar sphincters and thus would reverse pulmonary spasm (vasoconstriction) [9]. This might also promote healing of the lung parenchyme [10]. Elimination of the pumping mechanisms reduces the danger of trauma to the blood components.

Pumpless arteriovenous perfusion might thus find some application in patients suffering from chronic obstructive pulmonary disease with recurrent episodes of acute respiratory failure secondary to hypoventilation and CO_2 retention. New developments on the way, such as the manufacture of cannulas for rapid percutaneous insertion in the blood vessels and surface heparinized equipment, thus favoring the elimination of systemic heparinization [11], would still futher simplify this mode of perfusion and make it safer.

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We would like to extend our gratitude to Nicole Martineau for her secretarial work.

References

1. Gattinoni L, Kolobow T, Tomlinson T, et al. Low frequency positive pressure ventilation with extracorporeal carbon dioxide removal (LFPPV-ECCO$_2$R): an experimental study. Anesth Analg 1978;57:470–7.
2. Kolobow T. An update on adult extracorporeal membrane oxygenation—extracorporeal CO$_2$ removal. Trans Am Soc Artif Intern Organs 1988;34:1004–5.
3. Awad JA, Roy J, Brassard A, Caron WM. Arteriovenous perfusion with a disposable bubble oxygenator for the temporary support of respiration. Ann Thorac Surg 1968;6:535–46.
4. Awad JA, Morin PJ. Arteriovenous partial perfusion. In: Zapol WM, Qvist J, eds. Artificial lungs for acute respiratory failure. New York: Academic Press, 1976:329–43.
5. Nolte SH, Jonitz WJ, Grav J, Roth H, Assenbaum ER. Hemodialysis for extracorporeal bicarbonate/CO$_2$ removal (ECBicCO$_2$R) and apneic oxygenation for respiratory failure in the newborn. Theory and preliminary results in animal experiments. Trans Am Soc Artif Intern Organs 1989;35:30–4.
6. Barthelemy R, Galletti PM, Trudell LA, et al. Total extracorporeal CO$_2$ removal in a pumpless artery to vein shunt. Trans Am Soc Artif Intern Organs 1982;28:354–8.
7. Gille JP, Saunier C, Baluais G, et al. Extracorporeal CO$_2$ removal by hemodialysis. ASAIO J 1984;7:80–5.
8. Griffith BP, Borovetz HS, Hardesty RL, Hung TK, Bahnson HT. Cardiopulmonary dynamics during arteriovenous perfusion: cardiac output, pulmonary arterial resistance and right ventricular stroke work. Ann Thorac Surg 1978;29:49–56.
9. Bohr DF. The pulmonary hypoxic response. Chest 1977;71:244–8.
10. Andrews AF, Toomasian J, Oram A, et al. Total respiratory support with venovenous ECMO. Trans Am Soc Artif Intern Organs 1982;28:350–3.
11. Brindslev L. Adult ECMO performed with surface-heparinized equipment. Trans Am Soc Intern Organs 1988;34:1009–13.

DISCUSSION

DR JOSEPH B. ZWISCHENBERGER (Galveston, TX): As you know, Ted Kolobow and Luciano Gattinoni have taught us that CO$_2$ extraction and oxygenation have entirely different physiological mechanisms of respiratory support. I was wondering if you measured CO$_2$ production or oxygen consumption in your animals.

DR AWAD: No. What we actually did was to maintain a constant arterial CO$_2$ level and calculate the extraction from the membrane oxygenator. In one series it was maintained at an arterial P_{CO_2} of 40 mm Hg. The next series was at about 80 to 90 mm Hg and, as in the upper curve of Figure 9A, at 130 mm Hg. We calculated CO$_2$ extraction from the membrane oxygenators during the 7 days.

DR RICHARD E. CLARK (Pittsburgh, PA): Did you have to change the oxygenator at all during these experiments, and were there any differences between the oxygenators in terms of performance in removing carbon dioxide?

DR AWAD: No, we didn't have to change them at all, except in 1 case where there was an accident during one perfusion. The membrane oxygenator remained in place all the time for the 7 days. As far as oxygenation, most membrane oxygenators were made for perfusions of up to 5 L, thus with the lower flows we used, the outlet oxygen tension was around 600 or 700 mm Hg. Carbon dioxide extraction was very good up to 7 days without problem.

The only difference between the various membrane oxygenators was that the Maxima had lower resistance to blood flow and we could get flow rates up to 2,300 mL, which was definitely better than with the others. The other difference is that with the Capiox and with the Bentley, at the end of the perfusions when we washed them there were some blood clots inside the capillaries because the blood in these devices circulates inside the capillaries, whereas with the Maxima membrane oxygenator the blood was outside. Thus we did not have such a problem with the Maxima membrane oxygenator.

Benefit From Combining Blood Conservation Measures in Cardiac Operations

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Conventional blood conservation techniques have been insufficient to decrease transfusion needs in increasingly complex cardiac operations. To evaluate combinations of conservation techniques, 300 patients were divided into three equal groups. Group 1 had intraoperative autotransfusion and return of mediastinal drainage for 4 hours postoperatively. Group 2 had these measures plus intraoperative plasmapheresis. These two groups were given a transfusion for a hematocrit of less than 0.21 on cardiopulmonary bypass. Group 3 was treated with the same measures as group 2 but did not receive transfusions while on pump unless the hematocrit decreased to less than 0.15. The percentage of patients in each group given transfusions in the operating room was 34% in group 1, 28% in group 2, and 7% in group 3 ($p < 0.05$). The percentage of all patients receiving transfusions during hospitalization was 68% in group 1, 36% in group 2 ($p < 0.05$), and 18% in group 3 ($p < 0.05$). Average total units transfused were 2.16 ± 0.25 in group 1, 0.7 ± 0.15 in group 2 ($p < 0.05$), and 0.37 ± 0.07 in group 3 ($p < 0.05$). The perioperative morbidity rates including myocardial infarctions and strokes were similar. There were no deaths in group 3. Combining complementary conservation measures is effective in reducing homologous blood transfusions, and the need for transfusion can be safely reduced by allowing profound hemodilution during bypass.

(Ann Thorac Surg 1991;51:541–6)

Publicity regarding transfusion-related diseases has stimulated efforts to reduce homologous blood transfusions (HBTs). However, steadily rising HBT rates demonstrate that conventional blood conservation techniques are inadequate to accommodate the increasingly complex population referred for cardiac operations. At one institution known for leadership in blood conservation, the average HBTs per patient undergoing cardiac operations increased from 0.3 unit to 1.8 units over a 5-year period [1]. A recent survey [2] of 32 centers in England revealed that patients undergoing cardiac operations currently receive an average of more than 5 HBTs.

Initial studies [3–5] indicate that intraoperative plasmapheresis combined with other conservation measures reduces the need for HBTs in the population currently having cardiac surgical procedures. Also, evidence suggests that lowering the transfusion trigger while the patient is on cardiopulmonary bypass in the operating room may further reduce HBTs [6] and is safe [7]. The present study examines the effects on the requirement for HBTs of combining conventional blood conservation measures with intraoperative plasmapheresis and of combining conventional blood conservation measures with intraoperative plasmapheresis plus extreme intraoperative hemodilution.

Material and Methods

This retrospective study comprises 300 patients having initial coronary artery bypass procedures. They were divided into three study groups of 100 patients each, the three groups defined by two successive changes in our blood conservation program. Initially, our techniques included intraoperative autotransfusion, hemodilution on cardiopulmonary bypass to a hematocrit of 0.21 before transfusion, return of all pump blood, and reinfusion of mediastinal drainage for the first 4 hours postoperatively (group 1). Patients meeting the study criteria were assigned consecutively to this group beginning in July 1986. The dates the conservation techniques changed defined the beginning of groups 2 and 3. Once a change was instituted, the first 100 patients meeting the study criteria were assigned to that group. The first change (group 2) introduced intraoperative plasmapheresis to the previously used techniques. The second change (group 3) allowed hemodilution to a hematocrit of 0.15 on cardiopulmonary bypass rather than 0.21, while all other techniques used in group 2 remained constant. Patients with any abnormal preoperative clotting studies were excluded. These studies included prothrombin times, partial thromboplastin times, platelet counts, simplate bleeding times, and Lee-White clotting tests. Seventy variables indicating preoperative status, operative circumstances, and postoperative course were studied while the patients were hospitalized.

All operations were done by the same team using the same operative techniques. Membrane oxygenators, car-

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Table 1. Characteristics of the Study Groups[a]

Variable	Group 1	Group 2	Group 3	p Value
Age (y)	61.6 ± 0.9	59.8 ± 1.0	60.2 ± 1.1	0.39
Sex (male = 1)	72%	76%	75%	0.77
Preop weight (kg)	79.1 ± 1.6	81.5 ± 1.5	85.5 ± 1.8[b]	0.02
Pump time (min)	102.6 ± 3.6	103.7 ± 4.5	97.5 ± 3.4	0.44
One IMA	35%	26%	28%	0.34
Both IMAs	55%	68%	54%	0.08

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] Significance: $p < 0.05$ versus group 1.

IMA = internal mammary artery.

dioplegia, and external cold saline solution in the pericardial space were used. The patient's core temperature was lowered to 28°C, and rewarming was continued to 37°C before discontinuation of bypass. Pediatric-sized amounts of blood were drawn for laboratory tests. Swan-Ganz catheters, which continuously measure venous oxygen saturation, were used, and laboratory monitoring tests were kept to a minimum.

Removal of platelet-rich plasma was started after insertion of central lines and was terminated either at the accumulation of 1,000 mL of plasma or at the administration of heparin sodium. A plasma separator (Haemonetics model 5000) was used. Volume replacement was routinely started with 5% albumin during plasmapheresis. The platelet-rich plasma, stored at room temperature, was reinfused when the sternum was closed. Ultrafiltration was used selectively in the three groups. Clotting factors and homologous platelets were transfused in actively bleeding patients when laboratory tests confirmed specific abnormalities.

The following indications for HBTs were strictly observed after the patients left the operating room. Patients younger than 70 years were given HBTs when the hemoglobin level was less than 70 g/L. Patients older than 70 years received transfusions when the hemoglobin level was less than 80 g/L. Patients with pulmonary failure, cerebral injury, or perioperative myocardial infarction had transfusions to raise the hemoglobin level to 100 g/L.

Comparisons between the three groups were performed primarily by analysis of variance, if significant. Otherwise, paired comparisons between groups were made using Student's t tests. Chi-square statistics compared categorical variables. Multivariate regression analyses were used when appropriate.

Results

Analyses of the preoperative variables known to affect the need for HBTs [7, 8] showed that the composition of the study groups differed slightly (Table 1). Age, sex, pump time, average number of bypass grafts, and percentage of internal mammary conduits were not significantly different between the three groups. However, the average preoperative weight of patients in group 3 was heavier than in group 1 ($p < 0.05$). When compared individually, the average weights of group 1 patients versus group 2 patients and group 2 patients versus group 3 patients were not significantly different.

Group 3 required significantly fewer HBTs in the operating room compared with both groups 1 and 2 ($p < 0.0001$) (Table 2). Although group 2 received fewer transfusions per patient, the difference in HBTs given in the operating room between groups 1 and 2 was not significant. After leaving the operating room, groups 2 and 3 received significantly fewer transfusions than did group 1 during the remainder of the hospital stay ($p < 0.0001$). Average clotting factors transfused did not differ significantly between the three groups, although group 1 received more clotting factors than did groups 2 or 3.

Statistical analyses of the number of days spent in the intensive care unit, on a mechanical ventilator, and in the hospital before discharge revealed no significant differences between the groups (Table 3). Mortality and morbidity rates were comparable in the three groups. (Table 4).

Comment

The effectiveness of combining multiple blood conservation measures is well documented [4, 5, 7, 9–12]. Specifically, acute normovolemic anemia combines well with methods that retrieve and reinfuse shed blood [13]. However, when using even multiple conventional techniques,

Table 2. Average Homologous Blood Transfusions in the Study Groups[a]

Variable	Group 1	Group 2	Group 3	p Value
HBTs in OR (U)	0.74 ± 0.12	0.46 ± 0.08	0.08 ± 0.03[b]	0.0001
HBTs in OR (% patients)	34	28	7	<0.0001
HBTs after OR (U)	1.42 ± 0.26	0.27 ± 0.07[c]	0.23 ± 0.07[c]	<0.0001
HBTs total (U)	2.16 ± 0.25	0.70 ± 0.15	0.31 ± 0.07	0.0001
HBTs total (% patients)	68	36	18	<0.0001
Clotting factors (U)	1.05 ± 0.4	0.39 ± 0.23	0.47 ± 0.4	0.17

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] Significance: $p < 0.0001$ versus groups 1 and 2. [c] Significance: $p < 0.0001$ versus group 1.

HBTs = homologous blood transfusions; OR = operating room.

Table 3. Comparison of Postoperative Variables

Variable	Group 1	Group 2	Group 3	p Value
ICU days	3.35 ± 0.60	3.80 ± 1.10	2.68 ± 0.40	0.57
Ventilator days	2.02 ± 0.60	1.15 ± 0.07	1.06 ± 0.03	0.53
Hospital days	9.34 ± 0.70	7.66 ± 0.30	9.05 ± 0.57	0.16
Operative weight gain (kg)	4.58 ± 0.25	3.83 ± 0.25	4.30 ± 0.25	0.11

ICU = intensive care unit.

other studies [10–14] report that an average of two to three HBTs are obligatory per procedure. By further reducing the need for HBTs, intraoperative plasmapheresis seems to augment conventional techniques well [4, 5, 15]. The present study presents a larger group of patients having plasmapheresis than we [5] reported previously with approximately the same average HBT requirements.

Overtransfusion with HBTs occurred when the same transfusion trigger (70 g/L or 0.21 hematocrit) was used in the operating room as was used postoperatively. The hematocrits of patients with lower preoperative red cell volumes frequently fell below the transfusion limit of 0.21 while the patient was on cardiopulmonary bypass. Postoperatively, after diuresis, the hemoglobin concentrations often increased above our normal transfusion limits, thus indicating intraoperative dilution had occurred rather than actual blood loss. This illustrates the hazard of using measurements that indicate concentrations rather than total available red cell mass.

The National Institutes of Health Consensus Conference of 1988 [1] suggested 70 g/L as a safe limit of postoperative normovolemic anemia provided certain precautions were heeded. Separately, Weisel and associates [16] cautioned against potential cardiac injury with a hemoglobin level of less than 7 g/L in cardiac patients postoperatively. These recommendations, however, were made for the awake patient after operation, who has quite different metabolic needs than the patient under anesthesia on cardiopulmonary bypass.

Table 4. Mortality and Morbidity in the Study Groups[a]

Variable	Group 1	Group 2	Group 3	p Value
Death	2	0	0	0.13
More than 2 days on ventilator	6	5	2	0.35
Return to OR	4	4	2	0.66
Coagulopathy	2	3	0	0.24
IABP	2	5	1	0.19
Periop MI	2	2	3	0.29
CVA	3	1	0	0.17
CNS confusion	4	4	2	0.66

[a] Data are shown as percentages.

CNS = central nervous system; CVA = cerebrovascular accident; IABP = intraaortic balloon pump; MI = myocardial infarction; OR = operating room.

Reduction of HBTs on cardiopulmonary bypass began almost three decades ago with the substitution of nonblood pump prime [17]. Cosgrove and associates [7] allowed a hematocrit of 0.15 for patients on cardiopulmonary bypass before giving transfusions. These authors reported excellent clinical results in a series of more than 400 patients having cardiac procedures. Others [6, 13] have reported similar levels of extreme hemodilution on pump without deleterious effects. In 17 pediatric patients, hemodilution on cardiopulmonary bypass was allowed to an average hematocrit of 0.11, and the patients sustained no apparent harm [18]. In these studies, the lowered hematocrits were intentionally created by intraoperative phlebotomy before the patients were put on bypass. In contrast, in the present study, only plasma was withdrawn.

Experimental studies [19] using pigs verified the safety of a 0.15 hematocrit when discontinuing cardiopulmonary bypass at normothermia. Anesthetized primates ventilated on room air did not increase systemic lactate production or decrease oxygen consumption until the hematocrit was lowered to less than 0.10 [20].

In the present study, only 7 patients in group 3 whose hematocrits fell lower than 0.15 were given transfusions in the operating room. No detrimental effects were seen in these patients or in 18 others in group 3 whose hematocrits fell to less than 0.21.

Studies that lower oxygen-carrying capacity to a level that induces physiological derangements help define the safe limits of acute normovolemic anemia. These data are from normothermic preparations that are not supported by extracorporeal circulation. In the anesthetized primate, neurological function deteriorates at a hematocrit of less than 0.10, and reinfusion of erythrocytes does not result in immediate recovery [21]. At a 0.10 hematocrit, cardiac lactate production, which indicates onset of anaerobic metabolism, starts in primates [20]. In studies using dogs with a 0.20 hematocrit, Geha [22] noticed no detrimental cardiac effects. However, he suggested that adaptive increases in coronary flow resulting from anemia used part of the coronary reserve flow that would otherwise be available. He warned against a severe anemia in situations where coronary artery stenosis was present or where higher than usual cardiac work loads were necessary. Finally, left ventricular function curves were adversely affected by combining acute anemia with experimentally produced coronary artery stenosis [23].

As others have reported, we found that lowering the transfusion trigger on cardiopulmonary bypass to a 0.15 hematocrit did not have demonstrable adverse effects. Also, the adjustment eliminated overtransfusion of patients who had lower preoperative red cell volumes. The addition of intraoperative plasmapheresis plus lower indications for HBTs significantly improved blood conservation. Also, as others [6, 18] have noted, extreme hemodilution in the operating room was safely tolerated.

Theoretically, excessive reduction of the plasma osmotic pressure can increase complications. Successive hemodilution and reduction of colloid pressure increases cardiac extravascular fluid [24]. In studies using dogs, investigators [25] found that lowering the plasma oncotic pressure to 50% of normal dramatically decreased the pressures tolerated before lung water increased. Although no harmful clinical effects were observed, total body water of individual patients was significantly increased without the addition of colloid when hemodilution was used [26]. In the present study, 25% to 50% of autologous plasma proteins were removed temporarily during plasmapheresis. In addition, allowance of extreme hemodilution further reduces the oncotic pressure. To avoid possible untoward effects, the plasmapheresate was replaced with 5% albumin as it was removed, and 50 g of albumin was added to the pump prime.

Continual improvement in blood surveillance methods should reduce the danger of exposure to HBTs in the future. However, blood remains a limited resource worthy of conservation attempts, particularly in areas of high use such as cardiac surgery. Complementary blood conservation techniques can achieve reductions in HBTs that would not otherwise be possible. Specifically, combining blood conservation methods with normovolemic anemia can safely decrease the requirements for HBTs in patients having a cardiac operation.

References

1. Cosgrove DM. Red cell transfusion in heart surgery. Consensus statement from the Perioperative Red Cell Transfusion Consensus Conference. Bethesda, MD: National Institutes of Health, June 27–29, 1988.
2. Russell GN, Peterson S, Harper SJ, Fox MA. Homologous blood use and conservation techniques for cardiac surgery in the United Kingdom. Br Med J 1988;297:1390–1.
3. Harke H, Tanger D, Frust-Denzer S, Papachrysanthov C, Bernhard A. Effect of preoperative separation of platelets on the postoperative blood loss subsequent to extracorporeal circulation during open heart surgery. Anaesthesia 1977;26:64–71.
4. Giordano GF, Rivers SL, Chung GKT, et al. Autologous platelet-rich plasma in cardiac surgery: effect on intraoperative and postoperative transfusion requirements. Ann Thorac Surg 1988;46:416–9.
5. Jones JW, McCoy TA, Rawitscher RE, Lindsley DA. Effects of intraoperative plasmapheresis on blood loss in cardiac surgery. Ann Thorac Surg 1990;49:585–90.
6. Dale J, Lilleaasen P, Erikssen J. Hemostasis after open-heart surgery with extreme or moderate hemodilution. Eur Surg Res 1987;19:339–47.
7. Cosgrove DM, Loop FD, Lytle BW, et al. Determinants of blood utilization during myocardial revascularization. Ann Thorac Surg 1985;40:380–4.
8. Giordano GF Sr, Giordano GF Jr, Rivers SL, et al. Determinants of homologous blood usage utilizing autologous platelet-rich plasma in cardiac operations. Ann Thorac Surg 1989;47:897–902.
9. Cosgrove DM, Thurer RL, Lytle BW, Gill CG, Peter M, Loop FD. Blood conservation during myocardial revascularization. Ann Thorac Surg 1979;28:184–9.
10. Nataf P, Jault F, Vaissier E, et al. Systematic perioperative use of an autotransfusion system in heart surgery: a prospective and comparative study in 283 patients. Arch Mal Coeur 1989;82:1869–73.
11. Dietrich W, Barankay A, Dilthey G, et al. Reduction of blood utilization during myocardial revascularization. J Thorac Cardiovasc Surg 1989;97:213–9.
12. Tyson GS, Sladen RN, Spainhour V, et al. Blood conservation in cardiac surgery. Preliminary results with an institutional commitment. Ann Surg 1989;209:736–42.
13. Bormann BV, Boldt J, Kling D, et al. Kombinierte Autotransfusion in der Herzchirurgie. Dtsch Med Wochenschr 1987;112:1887–92.
14. McCarthy PM, Popovsky MA, Schaff HV, et al. Effects of blood conservation efforts in cardiac operations the Mayo Clinic. Mayo Clinic Proc 1988;63:225–9.
15. Boldt J, Von Bormann B, Kling D, et al. Preoperative plasmapheresis in patients undergoing cardiac surgical procedures. Anesthesiology 1990;72:282–8.
16. Weisel RD, Charlesworth DC, Mickleborough LL, et al. Limitations of blood conservation. J Thorac Cardiovasc Surg 1984;88:26–38.
17. Cooley DA, Beall AC Jr, Grondin P. Open-heart operations using disposable oxygenators, 5 percent dextrose prime and normothermia. Surgery 1962;52:713–9.
18. Buckley MJ, Austen WG, Goldblatt A, Laver MB. Severe hemodilution and autotransfusion for surgery of congenital heart disease. Surg Forum 1971;22:160–2.
19. Moores WY. Oxygen delivery during cardiopulmonary bypass. In: Utley JR, Ashleigh EA, eds. Pathophysiology and techniques of cardiopulmonary bypass, vol 1. Baltimore: Williams & Wilkins, 1982:1.
20. Wilkerson DK, Rosen AL, Gould SA, et al. Oxygen extraction ratio: a valid indicator of myocardial metabolism in anemia. J Surg Res 1987;42:629–34.
21. Nagao S, Roccaforte P, Moody RA. The effects of isovolemic hemodilution and reinfusion of packed erythrocytes on somatosensory and visual evoked potentials. J Surg Res 1978;25:530–7.
22. Geha AS. Coronary and cardiovascular dynamics and oxygen availability during acute normovolemic anemia. Surgery 1976;80:47–53.
23. Case RB, Berglund E, Sarnoff SJ. Changes in coronary resistance and ventricular function resulting from acutely induced anemia and the effect thereon of coronary stenosis. Am J Med 1955;18:397–405.
24. Laks H, Standeven J, Blair O, et al. The effects of cardiopulmonary bypass with crystalloid and colloid hemodilution on myocardial extravascular water. J Thorac Cardiovasc Surg 1977;73:129–38.
25. Guyton AC, Lindsey AW. Effect of elevated left atrial pressure and decreased plasma protein concentration on the development of pulmonary edema. Circ Res 1959;7:649–57.
26. Hallowell P, Bland JHL, Dalton BC, et al. The effect of hemodilution with albumin or Ringers' lactate on water balance and blood use in open-heart surgery. Ann Thorac Surg 1978;25:22–9.

DISCUSSION

DR ROBERT M. SADE (Charleston, SC): Were these groups prospectively randomized, how were they selected, and over what time period did the study take place?

DR JONES: They were not prospectively randomized, but were selected as sequential groups of 100 consecutive patients over a time period of 2½ years.

DR PAUL A. KURLANSKY (Miami, FL): I have two questions. What was the age range and the median age of your patients? Also, what was your threshold or your indication for transfusing patients postoperatively? I would further like to say that I very much enjoyed the paper. I think your techniques are excellent. Many of them we have found to be very useful in our own practice.

DR JONES: Thank you very much. The average age in the two groups was approximately 60 years. Approximately 25% of these patients were older than 70 years of age.

We transfused patients at a hemoglobin level of 70 g/L after leaving the operating room for patients under 70 years of age. We transfused patients 70 years old or older at a hemoglobin level of 80 g/L. Those patients who had perioperative infarctions, pulmonary failure, or brain injury were transfused at a hemoglobin level of 100 g/L.

DR HENDRICK B. BARNER (St. Louis, MO): What was the incidence of usage of single and bilateral internal mammary artery grafts?

DR JONES: We used bilateral mammary arteries in approximately 55% of these patients, and the overall vein use ranged only about 10% to 15%.

DR ROBIN W. HOWE (Paducah, KY): You mentioned all your patients received autotransfusion or reinfusion of shed mediastinal blood after operation. What was the volume or the average volume in the first 4 hours that was reinfused? Did it differ among the three groups? And do you routinely check antithrombin-3 levels in patients preoperatively?

DR JONES: We have not in the past routinely checked antithrombin-3 unless the patient had a positive history that would be compatible with that.

The volumes varied, but generally were around 200 to 250 mL in the first 4 hours. We did not transfuse exceedingly small amounts like 50 mL or 100 mL, because of the risk/benefit ratio of such small amounts. The majority of patients would receive 200 to 250 mL. It seemed to be less in the patients in whom intraoperative plasmapheresis was performed, but measurements of the amounts were not done.

DR CARY J. LAMBERT (Dallas, TX): The originality of a concept is merely an ability to distinguish the relevant from the irrelevant. Surely Jones and associates have done that with this presentation.

There are only two reasons to ever give transfusion to any patient regardless of blood sources or blood availability. The first of these is to improve oxygen delivery, and the second is to correct a coagulopathy. We ought to learn to restrict transfusion usage to one or the other of these indications rather than base it on hematocrit or hemoglobin stabilizations with respect to red cells or on "rule of thumb shotgun" treatment in the absence of a diagnosis when there is a coagulopathy.

An acute oxygen need is signified by a venous oxygen saturation less than 55 mm Hg in an otherwise hemodynamically stable patient on respiratory support. Chronically it is to be correlated to the peripheral oxygen state of saturation in the absence of a reduced cardiac output, pulmonary shunts, etc, and especially with ambulatory and alimentational desaturation employing the digital oximeter.

Postperfusion coagulopathies have been extensively covered through other presentations. I wish only to emphasize the need to administer factors specifically and selectively rather than empirically.

Unless and until one accepts and practices postoperative normovolemia throughout a person's clinical course, one will not really nor readily reduce blood usage by the measures alluded to in this presentation, nor will you optimize the benefits affordably available to you in that regard.

A question relates to when and why to employ or not employ hemoconcentration "on bypass hemodialysis." We believe it is very helpful for patients undergoing operation who have intractable congestive heart failure, renal failure, excessive cardioplegia administration, both coronary heart failure and valvar heart disease, cachexia (as might be for a patient with cardiomyopathy undergoing transplantation), and finally the "little old lady syndrome." Once employed, the technique of hemodilution is quite useful as a method by which to collect the perfusate rather than to simply run it into the autotransfusion systems, thereby better preserving volume composition while avoiding crystalloid overload with its predisposition to the adult respiratory distress syndrome.

DR JONES: I agree with everything you have said.

DR VAHE S. YACOUBIAN (Los Angeles, CA): I wonder if your patients are in stable condition, if you are not doing operation on an urgent basis. You try to take a unit or two of blood before operation. Can you comment about that, about autotransfusion taken preoperatively?

DR JONES: Yes. We do not attempt this procedure on hemodynamically unstable patients or patients who are in the process of having infarctions. I would not put a patient at risk to avoid a transfusion that might give him or her a relatively small future complication rate. Also, we do not do this if we are doing a single-valve procedure because collecting the platelet-rich plasma requires a sufficient amount of time before the heparinization is done.

DR YACOUBIAN: What I mean is, in nonurgent cases, such as patients in stable condition who are coming electively for a coronary artery operation or a valve operation. Do you tend to take a unit of blood from patients in stable condition with adequate hematocrit before putting the patient on bypass and before giving heparin? This would be mostly in coronary bypass patients who are hemodynamically stable and who do not have left main disease. It would not be done in patients in unstable condition and in patients who need complicated procedures.

DR JONES: This was done at the time of operation. I do not know that it would be a good idea to try and take plasma the night before because the platelet function may not be optimal the next day. We are removing approximately one third of the patient's total platelet mass intraoperatively, so we have not considered removing additional platelets the night before operation. We do try to use autologous blood donations in probably 15% of patients, with them donating a unit of whole blood before operation. Also, we just finished a study in which we have given erythropoietin for 5 days before operation. In both of these efforts the patients' conditions have to be nonurgent.

DR SADE: This paper had some very nice data, but we must be careful in interpreting them because of the fact that these patients were not operated on concurrently. The groups were sequential over 2½ years, and many details of management other than the design of the study probably changed from one time period to the next. This weakens the validity of the results, in my opinion.

DR JONES: What you are saying is true. To obtain perspective, you must realize the amount of blood that is currently used in an average coronary case. In the United Kingdom there was a paper published last year that reported an average of more than 5 units of blood per coronary bypass. Most recent papers published in the United States report an average of 3 to 5 units of blood.

I think to have a group of consecutive patients such as reported in this paper with an average homologous transfusion of less than 1 unit points to the fact that with use of new technology we can combat increasing transfusion requirements. This is the point I was trying to make. We tried to compare the groups and ideally we would have randomized this, but we added changes in our conservation program sequentially, as I mentioned in the report, to our techniques over a period of time. These patients were extracted as consecutive groups that were comparable according to the different variables that have been shown to predict blood usage. I assume that because we have the same operative team and basically are using the same operative techniques, we could at least make a statement that if you combine multiple types of conservation measures you may get a summation of desirable effects. What you say regarding randomized versus nonrandomized studies is exactly true.

Notice From the Southern Thoracic Surgical Association

The Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Grand Cypress, Orlando, Florida, November 7–9, 1991. There will be a $250 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 7, 1991. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Members wishing to participate in the Scientific Program should submit an original abstract and one copy by May 15, 1991, to Frederick L. Grover, MD, Program Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267. Abstracts must be submitted on the Southern Thoracic Surgical Association abstract submission form. These forms may be obtained from the Association's office or in this issue of *The Annals of Thoracic Surgery*. All slides used during the presentation must be 35 mm. Manuscripts of accepted papers must be submitted to *The Annals of Thoracic Surgery* prior to the 1991 meeting or to the Secretary-Treasurer at the opening of the Scientific Session.

Applications for membership should be completed by July 1, 1991, and forwarded to F. Hammond Cole, Jr, MD, Membership Committee Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267.

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Thoracotomy in the Octogenarian

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Octogenarians are rarely referred for thoracic operations, presumably owing to the perceived morbidity of thoracotomy and the presumed frailty and limited life span of the 80-year-old patient. To determine if these concerns are valid, we reviewed our operative experience in 50 patients 80 years of age or older (mean age, 82.7 years; range, 80 to 91 years; 29 men, 21 women) undergoing thoracotomy between Nov 1, 1980, and May 1, 1990, for cancer (39 patients) and benign disease (11 patients). Procedures included 25 lobectomies (24 cancer, 1 abscess), 4 pneumonectomies (all cancer), 3 esophagectomies (1 perforation, 2 cancer), 3 explorations for cancer, 2 bullectomies, 12 wedge or segmental resections (5 open lung biopsies, 5 cancer, and 1 each for benign nodule and hemoptysis), and 1 thymectomy. Five patients (10%) were operated on emergently for massive hemoptysis (1), Boerhaave's syndrome (1), or rapidly progressive respiratory insufficiency (3) with an operative mortality of 80%. Mortality for elective cases was significantly lower (13%, $p < 0.01$). Major complications occurred in 19 patients (38%). Univariate analysis performed to identify predictors of operative mortality demonstrated no significant relationship between operative death and patient age, sex, type of operation, diagnosis of malignancy, or the presence of either cardiac disease or chronic obstructive lung disease. Twenty-three patients are alive 2 months to 5 years after thoracotomy. Actuarial survival for the 45 elective patients was 56% and 44% at 1 and 2 years, respectively. These data suggest (1) elective thoracotomy may be performed in the 80-year-old patient with elevated but acceptable morbidity and mortality, (2) urgent operation in a compromised octogenarian yields a prohibitive operative mortality and must be approached with caution, and (3) operative survivors may enjoy extended survival with reasonable function.

(Ann Thorac Surg 1991;51:547–51)

Due to the gradually increasing age of the American population there is a continuing growth in the absolute number and proportion of patients over 80 years of age, many of whom are in excellent health. Such patients are being referred for thoracic surgical intervention with increasing frequency. The purpose of this review is to determine outcome, risk factors, and advisability of thoracotomy in this elderly population.

Patients and Methods

The records of all patients undergoing thoracotomy by faculty from St. Louis University Medical Center were reviewed and the charts of patients aged 80 years or older were selected for the study. Demographic data extracted from a review of these patients' records included patient age, sex, admitting diagnosis, and the presence of serious medical problems including chronic obstructive pulmonary and cardiovascular disease (history of infarction, angina pectoris, or congestive heart failure). The priority of operation (elective versus urgent) was recorded. Postoperative data recorded included duration of postoperative hospitalization, operative mortality (defined as death within 30 days of operation or at any time during hospitalization), and complications. Follow-up information was obtained on all survivors during office visits or by telephone interviews with the patient, a relative, or physician.

Data were analyzed using the StatView II statistical software package (Brainpower, Inc, Calabasas, CA). A univariate analysis of continuous variables was performed using the Student's t test. A χ^2 test or $2 \times k$ contingency table was used to determine significance for discrete variables. A p value of less than 0.05 was considered significant. Survival curves were constructed using the actuarial method of Berkson and Gage.

Results

From November 1, 1980, through May 1, 1990, 50 patients 80 years of age or older underwent thoracotomy. There were 29 men and 21 women ranging in age from 80 to 91 years with a mean of 82.7 years. The preoperative diagnosis included malignant and benign disease: lung cancer, 35 patients (70%); interstitial infiltrates, 5 (10%); bullous emphysema with bronchopulmonary fistula, 2 (4%); esophageal cancer, 2 (4%); and lung abscess, solitary pulmonary nodule, malignant thymoma, tuberculosis with hemoptysis, Boerhaave's syndrome, and metastatic colon cancer, 1 each (2%). Concomitant medical diseases included chronic obstructive pulmonary disease in 16 patients (32%), history of congestive heart failure or infarction in 4 (8%), and a history of stroke in 3 (6%).

Surgical procedures performed included lobectomy or bilobectomy in 24 patients (48%), segmentectomy or

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wedge resection in 6 (12%), open lung biopsy in 5 (10%), pneumonectomy in 3 (6%), esophagectomy in 3 (6%), exploratory thoracotomy in 3 (6%), bullectomy and pleurodesis in 2 (4%), and sternotomy with thymectomy in 1 (2%). The remaining 3 patients underwent en bloc chest wall resection in conjunction with either segmentectomy (1), lobectomy (1), or pneumonectomy (1). Five patients underwent operation on an emergency basis for the treatment of Boerhaave's syndrome (esophagectomy), tuberculosis with hemoptysis (segmentectomy), or progressive respiratory insufficiency with infiltrates (3 open lung biopsies).

Twenty-three patients suffered postoperative complications. These were considered major complications in 19 patients (38%): respiratory insufficiency, 11 patients (22%); pneumonia, 3 (6%); prolonged air leak, 2 (4%); urinary retention requiring transurethral prostrate resection, 2 (4%); and wound infection, prolonged oxygen requirement, stroke, and pulmonary embolus, 1 each (2%).

Ten patients died for an overall operative mortality of 20%. One 88-year-old woman suffered an episode of sudden death at home on the 29th postoperative day (2 weeks after discharge) following the performance of a right middle lobectomy for metastatic colon cancer. The remaining 9 patients died during hospitalization. One patient suffered a pulmonary embolus on the tenth postoperative day after lobectomy for primary lung carcinoma. The remaining 8 patients experienced a variety of complications, but all eventually died of respiratory insufficiency. Two patients who underwent lung resection (1 pneumonectomy with chest wall resection, 1 lobectomy) died on postoperative days 28 and 50 after prolonged ventilator support. A third patient who underwent lobectomy for primary bronchogenic carcinoma died on the 87th postoperative day after prolonged, intermittent ventilator support. Another patient suffered a sudden cardiorespiratory arrest of unknown cause on postoperative day 9 after a lobectomy for carcinoma. The remaining four deaths occurred in patients having urgent operation. One patient with Boerhaave's syndrome died on postoperative day 20. Another patient, who underwent right superior segmentectomy for massive hemoptysis secondary to tuberculosis, suffered acute respiratory distress syndrome and died on the seventh postoperative day. The final 2 patients died on postoperative day 7 and 9 after open lung biopsies, which had been performed for progressive pulmonary infiltrates. Both were ventilator dependent before operation. Both failed to respond to therapy and died.

Univariate analysis was performed to determine predictors of operative mortality. Analyzed variables included age, sex, diagnosis (malignant versus benign), operative priority (urgent versus elective), operation performed, presence of chest wall involvement, history of cardiovascular disease, and history of chronic obstructive pulmonary disease. As illustrated in Table 1, the need for an urgent procedure was associated with an 80% operative mortality versus 13% mortality for elective procedures ($p < 0.01$). No other significant differences were detected.

Table 1. Analysis of Operative Mortality

Variable	Survivors	Nonsurvivors	p Value
Number	40	10	. . .
Age (y)	82.5 ± 2.5	83.8 ± 2.7	NS
Male sex	22 (55%)	7 (70%)	NS
COPD	11 (27%)	5 (50%)	NS
ASHD	4 (10%)	0 (0%)	NS
Malignancy	33 (82%)	6 (60%)	NS
Chest wall involvement	1 (2%)	2 (20%)	NS
Urgent	1 (2%)	4 (40%)	<0.01
Operation			NS
Major lung resection	23 (57%)	6 (60%)	
Segment or wedge	9 (22%)	3 (30%)	
Esophagectomy	2 (5%)	1 (10%)	
Miscellaneous	6 (15%)	0 (0%)	

ASHD = atherosclerotic heart disease; COPD = chronic obstructive pulmonary disease; NS = not significant.

The 40 operative survivors were followed up for a period of 2 months to 7.6 years with a mean follow-up of 17 months. At the time of last follow-up, 23 patients (46%) were alive. Seventeen patients (34%) have died since discharge owing to recurrent cancer in 12, cerebrovascular accident and congestive heart failure in 2 each, and myocardial infarction in 1 patient. The functional status of the 23 survivors is good, with 78% of patients (18/23) being in New York Heart Association class I or II. Figure 1 depicts the actuarial survival curves for all patients as well as separate curves for patients with benign and malignant disease.

Comment

The population of the United States is progressively aging, and the mean age will continue to rise throughout the remainder of the century [1]. However, these elderly patients are healthier and have a longer projected life span than at any other time in our history [2]. Despite this, there is a marked tendency toward nonoperative therapy in the elderly. The option of surgical intervention is often rejected by the patient, his or her family, or the

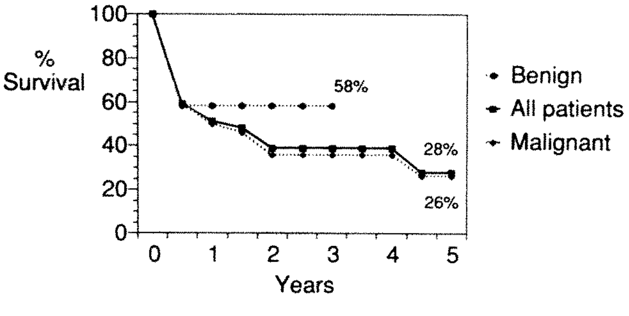

Fig 1. Actuarial survival curves for all octogenarian thoracotomy patients (squares)*, those with benign* (circle)*, and those with malignant* (diamond) *disease.*

physician because of the perception of frailty, the associated increased morbidity of operative intervention, or the limited life span of the patient. This trend is illustrated in a recent review of the National Cancer Institute Surveillance, Epidemiology and End Results Program in New Mexico. In this study it was demonstrated that as patient age increased, there was a progressive decline in the proportion of patients receiving definitive therapy for cancer [3].

Octogenarians presently comprise 3% of the American population [4]. In the past, advanced age has been a relative contraindication to surgical intervention. At one time, age beyond 70 years was prohibitory for thoracotomy [5]. However, over the past decade, septuagenarians have successfully undergone operative intervention with excellent long-term results for myocardial revascularization [6], valve replacement [7], and pulmonary resection [8]. Recently, authors have reported results of cardiac operations performed in octogenarians [9, 10]. Although mortality and morbidity were higher, most authors agreed that properly selected octogenarians are candidates for cardiac operations.

The issue of thoracotomy in septuagenarians for cancer [11] or other causes [12] was examined repeatedly in the 1970s and 1980s. Perhaps the pertinent issues were best expressed by Drs Yellin and Benfield [13] in an editorial dealing with operation for bronchogenic carcinoma in the elderly (septuagenarians). They identified four key questions to be answered in the controversy regarding thoracic surgery in the aged, all of which remain pertinent today in the discussion of octogenarians: (1) What are the consequences of nonoperative treatment for the underlying disease? (2) What is the life expectancy of the octogenarian? (3) What is the risk of thoracotomy? (4) What is the value of an operative approach in these problems?

Consequences of Nonoperative Intervention

Thirty-nine of our patients had a diagnosis of malignancy as their primary operative indication, with the lung being the most common organ of origin. It has been demonstrated that the relative mortality rate for lung cancer increases progressively with age, a fact likely due to the high incidence of concomitant medical diseases and the limited functional reserve found in this population [14]. Unfortunately, lung cancer in the elderly is an aggressive and highly lethal disease. Elderly patients with lung cancer treated nonoperatively have a limited life expectancy with only 7% alive at 1 year [15]. A similar prognosis was probable in the other malignant diseases in our patient series (ie, thymoma, esophageal cancer). It is highly unlikely that nonoperative therapy in these elderly patients with aggressive malignancies would have yielded any 5-year survivors.

The underlying pathology and its prognostic implications should also be considered in the 11 cases of benign disease. Three of the 11 patients (2 bronchopleural fistulas, 1 benign nodule) would have survived with nonoperative therapy although in 2, prolonged hospitalization with chronic chest tube drainage would have been required. The remaining patients with benign pulmonary pathology underwent thoracotomy for the purpose of diagnosis (5 patients with progressive pulmonary infiltrates) or had potentially lethal conditions that failed a trial of conservative therapy (1 Boerhaave's syndrome, 1 abscess with empyema, and 1 massive hemoptysis). Such patients find themselves "between a rock and a hard spot" and have little to lose by a "salvage" thoracotomy in an attempt to diagnose or treat their otherwise fatal diseases.

Life Expectancy

The projected life expectancy for the octogenarian patient in the United States is approximately 8 years [4], thus the limiting survival factor in elderly patients is not their projected life span but rather their underlying disease (malignant or otherwise) for which operation is being considered.

Risks of Thoracotomy

It has been established that increased age is a significant risk factor for operation in general [16, 17] and specifically for thoracotomy [8, 11, 18]. Careful patient selection and improvements in anesthetic management, surgical technique, and postoperative care have gradually decreased the magnitude of operative risk in the elderly. In the 1960s and 1970s operative mortalities of 12% to 20% were reported for thoracotomy with lung resection in septuagenarians [5, 11, 19]. Reported death rates in this same group have gradually declined and are now in the range of 3% to 9% [8, 12, 18].

Our operative mortality of 13% for elective thoracotomy in octogenarians appears analogous to the early septuagenarian experience. Several of our elective operative deaths arose from an aggressive approach taken in the early 1980s (evidenced by the 3 patients undergoing en bloc lung and chest wall resection). Since that time, better patient selection has produced improved results with only two deaths in the 25 thoracotomies performed since 1987 (1 pulmonary embolus, 1 respiratory insufficiency), yielding an operative mortality of 8% in that time period. It is likely that, as in the septuagenarian experience, more stringent patient selection and improved perioperative management will allow a continued decline in mortality figures.

Value of Operations

The 1- and 5-year actuarial survival rates for patients undergoing thoracotomy for malignant disease are 50% and 26%, respectively, figures unlikely to be matched by nonoperative therapy (see Fig 1). Interestingly, our 5-year survival figure is not dissimilar to those reported for septuagenarian patients by Breyer [12] (27%), Kirsh [11] (30%), Yellin [13] (35%), Sherman [8] (36%), and their associates.

Our 11 patients with benign disease had a 3-year actuarial survival of 58%. The 1 patient who underwent biopsy of a benign nodule would certainly have been better served without operation. The 4 patients who died (1 with Boerhaave's syndrome, 1 with hemoptysis, 2 with respiratory insufficiency and progressive pulmonary infiltrates) would almost certainly have had the same outcome without operation. The remaining 6 patients benefited either by obtaining a diagnosis (3 open lung biopsies) or by receiving successful treatment in the face of failed conservative therapy (1 with lung abscess and empyema, 2 with pneumothoraces and bronchopleural fistulas). All 7 patients survived.

Our experience suggests that, from the medical perspective, selected patients 80 years of age and older are viable operative candidates. Although they have increased operative morbidity and mortality, they will frequently benefit from surgical intervention with regard to both increased survival and improved quality of life. Our beliefs are well expressed by the following quote from Yellin and Benfield [13]: "Therapeutic nihilism is not defensible."

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References

1. US Department of Commerce. Statistical abstract of the United States. Washington, DC: Government Printing Office, 1981.
2. National Center for Health Statistics. Changes in mortality among the elderly. United States, 1970–78. Vital and Health Statistics, Series 3, No. 22. DHHS publication No. (PHS) 82-1406. Washington, DC: US Government Printing Office, March 1982.
3. Samet J, Hunt WC, Key C, Humble CG, Goodwin JS. Choice of cancer therapy varies with age of patient. JAMA 1986;255: 3385–90.
4. Bureau of the Census. Projections of population of the United States by age, sex, and race: 1983–2080. Current population reports, Series P-25, No. 952, Washington, DC: Government Printing Office, 1984.
5. Weiss W. Operative mortality and five year survival rates in patients with bronchogenic carcinoma. Am J Surg 1974;128: 799–804.
6. Roberts AJ, Woodhall DD, Conti CR, et al. Mortality, morbidity and cost accounting related to coronary artery bypass graft surgery in the elderly. Ann Thorac Surg 1985;39:426–32.
7. Bessone LN, Pupello DF, Hiro SP, Lopez-Cuenca E, Glatterer MS. Surgical management of aortic valve disease in the elderly: a longitudinal study. Ann Thorac Surg 1988;46: 264–9.
8. Sherman S, Guidot CE. The feasibility of thoracotomy for lung cancer in the elderly. JAMA 1987;258:927–30.
9. Naunheim KS, Dean PA, Fiore AC, et al. Cardiac surgery in the octogenarian. Eur J Cardiothorac Surg 1990;4:130–5.
10. Tsai TP, Matloff JM, Gray RJ, et al. Cardiac surgery in the octogenarian. J Thorac Cardiovasc Surg 1986;91:924–8.
11. Kirsh MM, Rotman H, Bove EJ, et al. Major pulmonary resection for bronchogenic carcinoma in the elderly. Ann Thorac Surg 1976;22:369–73.
12. Breyer RH, Zippe C, Pharr WF, et al. Thoracotomy in patients over age seventy years. Ten year experience. J Thorac Cardiovasc Surg 1981;81:187–93.
13. Yellin A, Benfield JR. Surgery for bronchogenic carcinoma in the elderly. Am Rev Respir Dis 1985;131:197.
14. Rossing TH, Rossing RG. Survival in lung cancer: an analysis of the effects of age, sex, resectability and histopathologic type. Am Rev Respir Dis 1982;126:771–7.
15. Thompson-Evans EW. Resection for bronchial carcinoma in the elderly. Thorax 1973;28:86–8.
16. Harbrecht PJ, Garrison RN, Fry DE. Surgery in elderly patients. South Med J 1981; 74:594–7.
17. Turnbull AD, Gundy E, Howland WS, et al. Surgical mortality among the elderly: an analysis of 4,050 operations. Clin Bull 1978;8:139.
18. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 1983;86:654–8.
19. Harviel JD, McNamara JJ, Straehly CJ. Surgical treatment of lung cancer in patient over the age of 70 years. J Thorac Cardiovasc Surg 1978;75:802–5.

DISCUSSION

DR RICHARD B. McELVEIN (Birmingham, AL): Dr Naunheim and his colleagues have presented an interesting series of patients who, as you have heard described, have undergone operation in their ninth decade of life. I think they should be congratulated on being able to do what they have done and have demonstrated to you. It shows that not only can they do it, but we can also take care of these patients.

I think in taking care of the elderly patients, and indeed any patient, operation is effective if you have serious physiology or pathophysiology that can be corrected by the operative procedure, in which case you can anticipate a better survival.

There is one deficit in the presentation, and that is to determine how many people in the same age group that they saw did not have any operations for a similar set of diseases, and what would be the natural history of an 85-year-old patient with pulmonary carcinoma that is not treated by lobectomy.

I would also like to ask if you would consider using the Karnofsky scale, which we find quite useful and a little bit more useful perhaps than the New York Heart Association classification because it does test the whole person. Finally, suppose you were back in St. Louis and they brought a patient into the emergency room today who started having his illness Wednesday and it was quite obvious he had Boerhaave's syndrome, and his birthday was the 11th of November, 1900. What would you do?

DR NAUNHEIM: First of all, with regards to pathophysiology, the majority of our patients had cancer that, if not treated surgically, had a very poor chance for cure. In such patients, a surgical procedure, even one with the morbidity such as thoracotomy, provides almost the only chance for cure. This is especially true in small asymptomatic cancers, found in about half of our patients. Most of the remaining patients were symptomatic from diseases other than cancer, and the thoracotomies were diagnostic, not therapeutic. Those patients with open lung biopsies, for example, underwent diagnostic thoracotomies. We did not expect all these patients to get better just as a result of our thoracotomy findings, but it does benefit a finite number of patients.

We did actually use the Karnofsky score and it may indeed, as Dr McElvein suggested, be a better representation of the patient's functional status. We observed that 75% to 80% of the patients had an excellent functional status—living at home, able to undertake their activities of daily living with little or no assistance.

Finally, with regard to that 90-year-old patient with Boerhaave's syndrome who is 48 hours out from perforation, the first thing I would do is look up Dr McElvein's name in the phone book and give him a call. He gave us an excellent lecture in the postgraduate course on complex benign disease, and certainly he knows better than I what the medical answer is. You do what you can to save the patient's life and to maximize his survivability and functional status.

But I think the intent of Dr McElvein's question is not so much medical, but rather somewhat more philosophical and practical. I think you also have to look at two other issues, one being the ethical aspects of operation in this patient group and the other being socioeconomic ramifications. As regards the ethical aspects, if the patient and his or her family really understand the risks and they wish to proceed with operation, and the patient has a cancer that is otherwise going to be fatal, then operation should be performed. We believe that as long as they understand what they are facing and we think that they have a good chance to tolerate the operation, we are ethically bound to go ahead with the surgical procedure.

With regard to socioeconomics, this country cannot afford to spend that kind of money necessarily on elderly patients such as this. Luckily, that is not my decision, but we also as physicians, I think, have a hard time refusing that kind of care to these patients. Certainly we deliver care to patients with acquired immunodeficiency syndrome and *Pneumocystis carinii* pneumonia. We do open lung biopsies on such patients who have mean life spans shorter than these octogenarian patients. Esophageal cancer is another good example where there is likely to be a 5-year survival less than we observed in this study. If we are providing care for such patients, I think we are going to have a hard time refusing it to "healthy" 80-year-old patients on the basis of age alone.

DR HARVEY I. PASS (Bethesda, MD): Can you just talk a little bit about the preoperative evaluation? For example, do you routinely do echocardiography, or do you routinely do pulmonary function tests or ventilation-perfusion scans? Do you change your preoperative work-up to suit this age of patient to try and make yourself feel better, and at least to know what you are getting into?

DR NAUNHEIM: Yes, we actually do. My standard work-up for someone with lung cancer is a chest roentgenogram, bronchoscopy, computed tomographic scan, pulmonary function test, and baseline blood gas measurement. Many of these patients in whom I am contemplating what for them is a significantly morbid procedure will have multiple aches and pains. I usually get a bone scan for these patients. If they have any neurological symptomatology at all, one should obtain magnetic resonance imaging. The worst thing you can do is operate on these patients and find out 6 months later that the operation is futile. Although we often do a good deal more, the standard work-up is the pulmonary function test, blood gas measurements, computed tomographic scan, and bronchoscopy.

DR ERIC L. CEITHAML (Jacksonville, FL): I would like you to address the issue of those patients over 80 years of age who have refused operation and are treated with radiation therapy.

DR NAUNHEIM: Dr McElvein asked this and I am sorry I forgot to answer it.

Actually, first of all, for our own institution, we tried to look up the number of octogenarian patients who had come in both with lung cancer and with benign diseases that could be treated with thoracotomy. The problem is that getting those data was next to impossible, because the coding was so poorly done. Back in the early 1970s and 1980s, the classification used by our hospital grouped together all patients older than 70 years of age and we could not abstract those lung cancer patients 80 years of age or older.

As to radiation therapy for these patients, these are very fragile patients and they do not tolerate radiation therapy well. Daily transportation is difficult for them and they do not tolerate the side effects very well. If one leaves the patient with a lung cancer untreated, the only data that I know for elderly patients is that approximately 10% of them will survive 1 year. But that, once again, is a figure from back in the 1970s, and I do not know if that is really a valid figure today. In general, these patients do not tolerate radiation therapy well.

DR J. B. ZWISCHENBERGER (Galveston, TX): Did you alter your operative technique for these older patients, using muscle-sparing incisions, rib resection, or any other maneuvers you can tell us about?

DR NAUNHEIM: More recently, we have been trying to use muscle-sparing thoracotomies, especially for those lesser procedures. The drainage procedures and the open lung biopsies have always been done through 5-cm incisions.

I think more important than changing our operative technique is probably paying meticulous attention to the patient preoperatively and postoperatively.

Prospective, Randomized Trial of Palliative Treatment for Unresectable Cancer of the Esophagus

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To evaluate the best method of palliation for obstructing nonresectable squamous cell carcinoma of the mid or distal esophagus, 27 patients were prospectively randomized to one of three treatment arms: (1) esophageal intubation with an Atkinson tube (AT, 10 patients), (2) esophageal intubation followed by radiation therapy (AT/RT, 8 patients), and (3) endoscopic laser therapy followed by irradiation (L/RT, 9 patients). Pretreatment characteristics were similar in the three groups. There was no procedure-related mortality. There were eight total complications related to the tube and none related to laser treatment ($p = 0.02$). Mean survival was 119 days in the AT group, 72 days in the AT/RT group, and 169 days in the L/RT arm (p = not significant). Quality of survival was most dependent on swallowing ability, and the swallowing score increased by 2.3 units in the AT group, 1.8 units in the AT/RT group, and 1.4 units in the L/RT group (p = not significant). Adding RT to laser therapy significantly increased time in treatment (mean, 38.7 days) when compared with the AT group (mean, 12.5 days) ($p < 0.001$). However, only 1 patient required repeat laser ablation. It is concluded that AT and L/RT result in good palliation as measured by relief of dysphagia and survival time. However, morbidity of AT is significantly greater than that of L/RT. Laser and radiation therapy with a reduced total dosage of RT or with a change in fractionation schedule to limit treatment time is the preferred method of palliation.

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Squamous cell carcinoma of the esophagus is a devastating disease, and for the vast majority of patients, palliation is the only realistic option. For those patients with obstructing unresectable tumors, the form of palliation to relieve dysphagia is of utmost importance because life span is usually measured in weeks to months. The objective of palliation is the restoration of oral alimentation by the least invasive means possible and with low morbidity and mortality.

With this goal in mind, patients seen at the Medical University of South Carolina with obstructing, unresectable squamous cell carcinoma of the mid and distal esophagus were prospectively randomized to one of three palliative treatment arms: (1) esophageal intubation alone, (2) esophageal intubation followed by radiation therapy, and (3) endoscopic laser therapy followed by irradiation. Specific aims of the study were assessment of the morbidity and mortality of each form of treatment, time spent in the hospital and in treatment, the quality of palliation, and survival.

Material and Methods

From May 1, 1986, to April 30, 1990, 88 patients with mid and distal squamous cell carcinoma of the esophagus were evaluated at the Medical University of South Carolina, Charleston, SC. Forty-one of 55 unresectable patients had an obstructing intraluminal tumor. Twenty-seven patients were prospectively randomized to one of three palliative treatment arms: (1) insertion of Atkinson tube (AT) (AT group, 10 patients), (2) insertion of AT followed by radiation therapy (RT) (AT/RT group, 8 patients), and (3) laser treatment to establish a patent lumen followed by RT (L/RT group, 9 patients). The protocol was explained to the patient and informed consent was obtained by the principal investigator under the approval of the Institutional Review Board of the Medical University of South Carolina (January 21, 1986). Patients refusing randomization (4 patients) or having a tracheoesophageal fistula (3 patients) were treated in accordance with the physician's or patient's preference. In 7 cases it was not clearly documented why the patient was treated alternately.

Pretreatment Characteristics

The patient population consisted of 22 men and 5 women (M:F = 4.4:1) with all but 2 being black. Twenty-six patients recorded heavy cigarette use and 25 admitted to alcohol abuse. Dysphagia (27 patients) and cachexia (22 patients) were most common on presentation, followed

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Table 1. Pretreatment Characteristics of the Palliative Group

Variable	Group 1 (AT)	Group 2 (AT/RT)	Group 3 (L/RT)	*p* Value
Number of patients	10	8	9	
Mean age, years (range)	62.6 ± 10.6 (37–72)	61.0 ± 12.3 (49–77)	61.1 ± 16.1 (35–87)	NS
Duration of symptoms, months (range)	2.1 ± 2.1 (0.5–6)	2.1 ± 2.1 (1–7)	1.5 ± 0.6 (0.5–2)	NS
Average weight loss, kg (range)	11.8 ± 6.0 (5.4–22.5)	10.3 ± 6.0 (2.3–18)	12.0 ± 4.5 (4.5–15.8)	NS
Average tumor length, cm (range)	7.7 ± 1.8 (5–11)	8.7 ± 2.0 (5.5–12)	8.1 ± 3.4 (4–15)	NS
Degree of luminal obstruction				
<75%	0	2	1	
75%–90%	4	3	5	NS
>90%	6	3	3	
CT scan/biopsy				
Local tumor extension	9	6	8	NS
Distant metastasis	3	3	3	NS
Average Karnofsky performance status (range)	66.5 ± 26.3 (20–90)	76.9 ± 12.8 (50–90)	78.9 ± 11.7 (50–90)	NS

AT = Atkinson tube; AT/RT = Atkinson tube + radiation therapy; CT = computed tomographic; L/RT = laser therapy + radiation; NS = not significant.

by chest pain (6), nausea and vomiting (6), and regurgitation (5). The pretreatment characteristics of each group are summarized in Table 1.

Palliative Procedures

GROUP 1 (AT). The Atkinson tube (Olympus; KeyMed, Inc, Spring Valley, NY) was inserted by the method described by Ogilvie and associates [1]. A medium-diameter (internal diameter, 11.6 mm) short tube was inserted in 6 patients, a medium-diameter long tube in 1 patient, and a large-diameter (internal diameter, 12.9 mm) short tube in 3 patients. A postintubation chest roentgenogram confirmed the tube's position and excluded perforation. A Gastrografin swallow was done the next day before institution of eating. The patient was discharged with instructions to eat in an upright position, masticate food thoroughly, and drink carbonated beverages often with each meal.

GROUP 2 (AT/RT). After insertion of the AT (3 medium-diameter short, 1 medium-diameter long, 2 large-diameter short), radiation therapy to the esophageal tumor bed was given to a total dose of 45 Gy in 25 fractions.

GROUP 3 (L/RT). Ablation of intraluminal tumor was achieved using the neodymium:yttrium-aluminum-garnet laser (Model 8900; Cooper LaserSonics, Inc, Santa Clara, CA). Because of the degree of obstruction, the prograde approach was used in most instances. Laser therapy was continued until patency to at least full liquids was achieved. Total energy used per patient ranged from 417 to 15,461 J. Patency was achieved in an average of three sessions (range, one to six). The patient then underwent radiation therapy as given in group 2 to maintain the esophageal lumen.

Assessment of Palliation

The palliative modalities were assessed for initial success and ease of procedure, complications of treatment, immediate mortality related to the procedure, time in treatment and hospital, and survival. Quality of palliation was evaluated at monthly intervals by means of a graded questionnaire as proposed by Stoller and associates [2], which assessed pain, swallowing ability, sleep, leisure activity, and work status. Karnofsky performance status and weight were recorded at each visit.

Statistical Analysis

Tabular data are summarized by the mean ± standard deviation, as well as the range, for continuous variables. Categorical variables are reported as counts. Comparisons among the three groups were performed for continuous variables by analysis of variance and, when appropriate, pairwise *t* tests using Bonferroni significance levels. Categorical variables were compared using χ^2 tests and Fisher's exact test.

Results

In group 1 (AT), there were five tube-related complications. Tumor perforation occurred at the time of insertion in two instances. In one case, exploratory laparotomy was required for perforation at the gastroesophageal junction and an AT was repositioned to block the perforated tumor and anchored in a fashion similar to Celestin tube placement. In another case, complete fracture of tumor, probably during dilation, was suspected because of a postoperative fever and a chest roentgenogram revealing a pleural effusion. In both these cases, the AT sealed the perforation, and the patients were discharged from the hospital. Tube migration occurred in 1 patient, and the stent was easily removed endoscopically. This patient refused all further treatment and died while awaiting nursing home placement. Tube impaction occurred in 2 patients and clot and food were removed using the endoscope.

Further therapy was used in three instances in group 1. Rib pain in 1 patient was controlled by a short course of

Table 2. Palliative Treatment Results

Variable	Group 1 (AT; n = 10)	Group 2 (AT/RT; n = 8)	Group 3 (L/RT; n = 9)	*p* Value
Complications	5	8	0	<0.02[a]
Aborted procedure	0	2	1	
Further therapy required	3	1	1	
Mean survival, days (range)	119 ± 82 (6–228)	72 ± 62 (14–163)	169 ± 92 (14–293)	NS
Mean hospital days (range)	11.4 ± 12.3 (2–43)	. . .[b]	12 ± 6.8 (5–26)	NS
Mean time in treatment and hospital, days (range)	12.5 ± 11.7 (2–33)	. . .[b]	38.7 ± 10.2 (30–60)	<0.001
Mean increase in swallowing score (range)	2.3 ± 1.1 (1–4)	1.8 ± 1.0 (1–3)	1.4 ± 0.5 (1–2)	NS

[a] L versus AT. [b] See text.

AT = Atkinson tube; AT/RT = Atkinson tube + radiation therapy; L/RT = laser therapy + radiation therapy; NS = not significant.

irradiation. Approximately 3 months after AT placement, obstruction of the tube by overgrowth of tumor proximal to the stent developed in this same patient. Barium swallow showed a tracheoesophageal fistula. His tube was removed and a longer tube reinserted. He achieved good palliation for another 4 months. A second patient in group 1 underwent laser ablation of tumor that grew beyond the distal end of his tube 4 months after AT insertion.

In group 2 (AT/RT), the procedure was aborted in two instances after a guidewire could not be passed through the tumor. One patient sustained tumor perforation at the time of insertion that was successfully sealed by the Atkinson tube. Respiratory distress developed in another patient with massive tumor abutting the distal trachea a few days after AT insertion and required tracheostomy. Placement of the AT may have further compromised the tracheal lumen. He died during his course of RT. The AT migrated after completion of RT in 1 patient. Further therapy (RT and laser) was used in a patient for distal extension of tumor.

In group 3 there were no complications related to laser therapy. One attempt was aborted because the tumor was considered too infiltrative for successful and safe ablation. In 1 patient with a 15-cm tumor, obstruction with further tumor developed 3.5 months after laser treatment. Dilation and attempted AT placement were unsuccessful, and he died. Other than this patient, no one required repeat laser treatment.

Results are summarized in Table 2. There were eight total complications related to the tube and none related to laser treatment ($p = 0.02$). There was no procedure-related mortality, but 6 patients died in the hospital before finishing treatment (3 patients) or awaiting placement (3). These deaths were related to the advanced nature of the disease.

Disregarding aborted cases, the mean survival from the first day of treatment was 119 days in group 1 (AT), 72 days in group 2 (AT/RT), and 169 days in group 3 (L/RT). Further comparison with group 2 was hampered by the complication rate and early deaths. Patients in group 1 (AT) spent an average of 11.9 days in the hospital/treatment, and patients in group 3 (L/RT) had a mean treatment plus hospital time of 35.6 days. If only those patients who completed treatment are included, mean time in treatment and hospital was 12.5 days in group 1 (AT) and 38.7 days in group 3 (L/RT) ($p < 0.001$).

The quality of palliation as graded by the patient proved to be most dependent on swallowing ability. The swallowing score increased by 2.3 units in the AT group, 1.8 units in the AT/RT group, and 1.4 units in the L/RT group (p = not significant). In all patients in the L/RT group and in all except 1 patient having successful tube placement, a score of 4 (all soft food) or 5 (any food) was achieved. In group 1 (AT), 6 patients gained some weight, 1 failed to gain, and 2 patients did not have follow-up weights recorded. However, weight gain did not remain consistent and was not correlated with swallowing ability over time. This was also true in group 3 (L/RT), where 4 of 8 patients gained some weight. The average Karnofsky performance status improved modestly in both these groups (AT, 12 points; L/RT, 6 points).

Comment

More than half of the patients with dysphagia due to esophageal carcinoma have nonresectable disease either owing to metastasis or to extraesophageal local spread. The form and quality of palliation become very important to this group of patients whose overall life span is severely limited. Although the national incidence of esophageal cancer is low (5 per 100,000), the coastal area of South Carolina suffers an incidence considerably greater than the national average. The incidence of esophageal cancer in black men between 55 and 64 years of age living in the sea islands is 182 per 100,000, an increase that is approximately 45 times the national average [3]. Thus, the Charleston area offers a unique setting for the study of this disease. A review of the pretreatment characteristics of the patients included in this study reveals that they indeed had advanced disease and represented a challenge to palliation.

The quickest methods of restoring oral alimentation were chosen for initial treatment: endoscopic intubation and laser therapy. Radiation therapy was added to each of these groups to assess its contribution to survival and quality of life.

The rationale for the use of an endoesophageal prosthesis alone was based on its simplicity, one-stage procedure, and short hospitalization. We [4] had previously shown that endoscopic insertion of an AT could be performed with an immediate complication rate of 13%, mortality of 6%, and a mean hospital stay of 4 days, and that it could provide satisfactory relief of dysphagia in 81% of patients with a mean survival of 3.6 months. However, it should be noted that the late complication rate was 33%, which gives a total complication rate of 46%. This total rate was similar to that in the reported series of Chavy and associates [5] and their review of the literature. Minor complications were observed in 40% of patients and severe, life-threatening complications in 20%. Obstruction, mobilization, or deterioration of the prosthesis occurred in 33%. In a recent report of 100 endoscopic tubes placed in 95 patients, complications occurred in 36 patients and were fatal in 16 cases [6].

In our prospective study, there were eight complications related to the Atkinson tube, a total complication rate of 50%. There were no complications related to the laser, and this was statistically significant.

A review of reported series using palliative neodymium:yttrium-aluminum-garnet laser therapy for obstructing esophageal carcinoma [7] confirms an overall low complication rate of 13.2% per patient and less than 10% per treatment number. In a retrospective study of prosthesis versus laser for obstructive esophageal cancer, Buset and co-workers [8] reported for laser therapy a reduction in immediate complication rate from 13.8% to 3.5% and in late complications from 26.7% to 0%.

One patient in the L/RT group required further therapy 3.5 months after initial treatment. The lack of need for retreatment is attributed to the addition of RT. This finding is despite the initial intent only to achieve luminal patency to liquids before RT. Buset and co-workers [8] reported that repeat laser therapy was required in 32% of patients and a further 17.8% underwent intubation for long strictures, early recurrence, or frequent recurrences.

Survival was unaffected by the method of palliation. The addition of RT to AT insertion did not prolong the duration of palliation and probably contributed to the tube migration.

Although mean hospital days for the AT and L/RT groups were not significantly different, the total time spent in the hospital plus in treatment was significantly longer for the L/RT group secondary to the duration of RT. The increase in hospital days for the AT group as compared with our previous Atkinson study is attributed to complications and further therapy required.

Assessment of the quality of palliation includes a number of variables. Our scoring system was an attempt to be as objective as possible. The change and maintenance of swallowing ability affected the total score most significantly. Both weight gain and Karnofsky performance status improved modestly but were not meaningful indicators of palliation. Relief of dysphagia remained the single most important factor to the patient, and all three groups achieved good swallowing ability if treatment was successfully completed.

One can conclude from this prospective, randomized study that use of AT and L/RT results in good palliation as measured by relief of dysphagia and survival time. However, the morbidity of AT is significantly greater than that of L/RT. Adding RT to AT insertion does not add any beneficial advantages. Adding RT to laser treatment appears to prevent the need for repeat therapy, but it does significantly increase the total treatment time for the patient. These preliminary results should be confirmed by others. At present we favor treating patients with obstructing nonresectable esophageal carcinoma with initial laser therapy to achieve luminal patency and adding RT at a reduced total dosage or with a change in fractionation schedule to decrease time in treatment. Intraluminal brachytherapy may also play a role in reducing treatment time and is worthy of further investigation. We reserve the AT for patients with tracheoesophageal fistulas or for patients with obstructing external compression who have failed RT.

With continued effort to reduce treatment time, the combination of L/RT achieves the goals of palliation: relief of dysphagia with minimum morbidity, acceptable survival, and maintenance of quality of life.

References

1. Ogilvie AL, Dronfield MW, Ferguson R, Atkinson M. Palliative intubation of oesophagogastric neoplasms at fiberoptic endoscopy. Gut 1982;23:1060–7.
2. Stoller JL, Samer KJ, Toppin DI, Flores AD. Carcinoma of the esophagus: a new proposal for the evaluation of treatment. Can J Surg 1977;20:454–9.
3. Bates DC, Coston JC, O'Brien P, Sandifer SH. Carcinoma of the esophagus in South Carolina. JSC Med Assoc 1971;67:453–6.
4. Kratz JM, Reed CE, Crawford FA, Stroud MR, Parker EF. A comparison of endoesophageal tubes: improved results with the Atkinson tube. J Thorac Cardiovasc Surg 1989;97:19–23.
5. Chavy AL, Rougier PM, Pieddeloup C, et al. Esophageal prosthesis for neoplastic stenosis: a prognostic study of 77 cases. Cancer 1986;57:1426–31.
6. Fugger R, Nierderle B, Jantsch H, Schiessel R, Schulz F. Endoscopic tube implantation for the palliation of malignant esophageal stenosis. Endoscopy 1990;22:101–4.
7. Pass HI, Reed CE. Lasers in the management of upper aerodigestive malignancies. In: DeVita VT, Hellman S, Rosenberg SA, eds. Important advances in oncology 1990. Philadelphia: J.B. Lippincott, 1990:159.
8. Buset M, des Marez B, Baize M, et al. Palliative management of obstructive esophagogastric cancer: laser or prosthesis? Gastrointest Endosc 1987;33:357–61.

DISCUSSION

DR KAMAL A. MANSOUR (Atlanta, GA): I really enjoyed your presentation very much and I congratulate you for a job well done. The only thing I have to ask is, what is the place of palliative bypass operation in managing unresectable lesions? I noticed the absence of this type of operation in your series. We, at Emory, use this mode of treatment—admittedly not very frequently. We use the colon for high obstructive unresectable disease and the stomach to bypass lower lesions.

We follow the Claggett operation that was described some 20 years ago for lower fixed lesions obstructing the gastroesophageal junction. The fundus of the stomach is mobilized, brought through the hiatus, and anastomosed to the divided esophagus above the tumor, end-to-side. I would like to get your thoughts on this.

DR REED: These patients were not surgical candidates because they all had extremely advanced disease, and I think you can tell by the pretreatment characteristics that they were indeed a very hard group to palliate. We have used surgical bypass. One of the patients that was eliminated from this group had a tracheoesophageal fistula and was young, and we used a gastric pull-up to the neck for bypass in him. He got excellent palliation.

The majority of these patients are malnourished—some of them, in fact, are almost moribund when first seen in the hospital. I think we are dealing with an extremely advanced group and they would not tolerate operation well.

DR WILLIAM H. MESSERSCHMIDT (Johnson City, TN): One of my questions was somewhat similar to Dr Mansour's, but I have a little problem with denying a person resection for an esophageal carcinoma just on the basis of a computed tomographic scan, if I understood your slide correctly. The second question, is do you have any feeling on whether the radiation treatment actually adds anything to the therapy or whether laser and possibly repeat laser therapy for this might be adequate?

DR REED: In response to your first question, the computed tomographic scans indicated extremely bulky mediastinal disease; very extensive disease. I think if I had the time to show you the computed tomographic scans, you would understand what I am saying, although I agree with you. In any case, we always give the benefit of the doubt to the patient and he or she is put in our resectable protocol. But all of these patients had very advanced, bulky mediastinal disease on computed tomographic scan.

Your second question, I think, is interesting. Recently in a retrospective series that studied patients treated by laser versus the tube alone, repeat laser treatment was required in 32% of the patients and further therapy—most of the time an Atkinson tube—in another 18%. We were therefore very favorably surprised that by adding radiation therapy to our laser treatment we did not have to repeat the laser treatment. Many of our patients come from some distance. As they get more cachectic, it is harder for them to get to the hospital, and so we were gratified with the result. We attribute it to the radiation therapy, but I think that needs to be investigated further.

DR LEWIS WETSTEIN (Freehold, NJ): I am delighted there are other investigators who are attempting to find a solution to the problem of these extremely unfortunate patients with unresectable malignant esophageal obstruction.

We recently reported our data, and although we found that laser therapy is an excellent modality, as you just noted, it is unfortunately short-lived [1]. That is why we routinely, once we open the esophageal lumen, insert an endoesophageal prosthesis. However, the survival among our patients was only 3.3 months, which has caused us to presently evaluate radiotherapy. I am puzzled, because in our initial half-dozen patients we are not only finding it unrewarding, but it is exacerbating their dysphagia, with the patients now unable to tolerate anything. I would thus like to know if there are any suggestions I can take back to our radiotherapists that may improve our results.

DR REED: We found in all cases that the radiation therapy helped. In our laser treatment we only opened up the lumen to fluids; so we did not, if you will, over-laser them. I think one interesting question might be what is the use of intraluminal radiation treatment or brachytherapy in this group. We are interested in that to cut down treatment time, but we did not find that the radiation therapy made their dysphagia worse. It was exactly the opposite.

DR RICHARD B. McELVEIN (Birmingham, AL): I enjoyed the presentation very much, and I think people in the audience would like to know exactly which laser you used, because there are a number of different wavelengths available on the market, and how you actually delivered them. I would also be interested in knowing the number of treatments you used for each patient. We have had a fair amount of laser experience with esophageal carcinoma and we think that it is a useful method of palliating these people, albeit for a short period of time. One other technical point: when you use your laser treatment, do you try and go retrograde and work your way back or do you start at the top and work your way down, or does it vary depending upon whether you can get through?

DR REED: At our institution we have a Cooper LaserSonics model 8900, and that is what we use. The patient's treatments varied in number from one to six with a mean of three treatment sessions. We would prefer, obviously, to use the retrograde approach, but in almost all of this very badly obstructed group of patients we had to use the prograde approach. We were gratified that it only took a mean of three sessions to open them up.

Reference

1. Wetstein L, Kirby DF, Brenner A. Treatment of malignant esophagorespiratory fistula. Mil Med 1990;155:324–6.

Improved Lung Preservation With Cold Air Storage

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Conventional topical slush cooling limits lung transport to 4 to 6 hours. For this canine study of an alternate air cooling system, 37 canine lungs were removed: 24 were placed in plastic bags, and inserted in a Transplanthermm container at core air temperatures (n = 6 lungs each) of (A) 4°C, (B) 8°C, (C) 12°C, and (D) 20°C; 6 were stored conventionally in ice slush (E); and 7 were transplanted immediately (F). After 8 hours, the stored lungs were transplanted and the contralateral pulmonary artery was ligated. Survival, arterial oxygen tension, and extravascular lung water were monitored at 15 minutes and every hour for 4 hours. Four-hour survival was 100% in groups A, B, and F; 83% in group C, 50% in group D, and 17% in group E. The mean arterial oxygen tension at 1 hour was lower in group E (6.4 ± 2.4 kPa) than in group A (39.8 ± 13.2 kPa) ($p = 0.0002$) or in group F (42.0 ± 16.2 kPa) ($p = 0.0035$). Extravascular lung water in group E was higher at 15 minutes (15.44 ± 5.63 mL/kg) than in group A (3.76 ± 0.63 mL/kg) ($p = 0.0001$) and group F (4.69 ± 1.65 mL/kg) ($p = 0.003$). Cold air storage appears to provide better lung preservation than hypothermic immersion in ice slush.

(Ann Thorac Surg 1991;51:557–62)

Lung transplantation has become a viable option for patients with end-stage lung disease [1, 2]. A scarcity of suitable donor organs has limited the number of transplantations performed thus far. Improved methods of preservation could substantially increase the number of available donor organs.

The time limit for successful clinical lung preservation with topical cooling and hypothermic immersion has been 4 to 6 hours [3]. Various flush solutions, administered at the initiation of an ischemic period, have been tried in an attempt to improve preservation of the pulmonary parenchyma [4–8]. Continuous perfusion systems have also been tried but are not readily transportable and are therefore difficult to adapt to clinical transplantation [9]. Although, currently, lungs are routinely transported while in an ice-slush bath immersion at 0° to 4°C, improved lung function has been demonstrated after storage at 10°C [10]. In this study, we investigated the use of a transportable container that keeps the lung cool with air at a constant, controllable temperature.

Material and Methods

All animals were handled in accordance with standards for animal care and use in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Preparation of Donor Animals

Thirty-seven adult mongrel dogs weighing 18 to 22 kg were anesthetized with intravenously administered sodium pentobarbital (30 mg/kg of body weight), intubated, and placed on a volume-cycle respirator. A bilateral transverse anterior thoracotomy incision was made. The inferior and superior venae cavae were ligated, the heart was allowed to empty, and the left lung with a large left atrial cuff was then removed. The left bronchus was divided at the carina and left open. The left pulmonary artery was divided at the bifurcation. All lungs were cooled briefly with topical cold saline solution at 4°C immediately before storage. Four groups of six lungs each were wrapped in plastic bags, inserted in the Transplanthermm container (Cardicorp S.A., Switzerland), and stored for 8 hours at 4°C (group A), 8°C (group B), 12°C (group C), and 20°C (group D). Air temperature within the Transplanthermm container was adjusted by filling the water jacket with fluid at the desired temperature (Fig 1). Six additional lungs were wrapped in plastic bags, thereby preventing direct contact of the lung with the ice, and stored for 8 hours in an ice-slush bath (0° to 4°C) within a styrofoam cooler (group E). Seven additional lungs were cooled topically and then transplanted immediately after harvest to serve as controls (group F).

Preparation of Recipient Animals

Thirty-seven adult mongrel dogs weighing 18 to 22 kg were anesthetized with intravenously administered sodium pentobarbital (30 mg/kg of body weight), intubated, and placed on a volume-cycle respirator at a tidal volume

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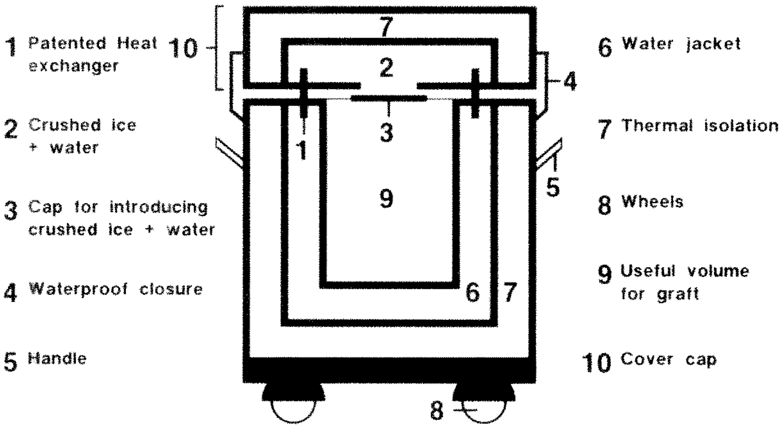

Fig 1. Component parts of the Transplanthermm container.

of 12 mL/kg, a respiratory rate of 8 to 12 breaths/min, and an inspired oxygen concentration of 100%. A central venous catheter was inserted through the jugular vein and an arterial cannula into the carotid artery. An Edwards Laboratory 96/020 catheter (Edwards Laboratory, Santa Ana, CA) was inserted into the right femoral artery and connected in sequence to a Waters D-401-A densitometer and a Waters 367 dye-dilution pump (Waters Instruments, Rochester, MN) for arterial blood withdrawal during measurement of extravascular lung water (EVLW).

A bilateral transverse anterior thoracotomy incision was made, and the right main pulmonary artery and right main bronchus were isolated. The left hilum was then dissected and a left pneumonectomy performed with long stumps being left on the artery, veins, and bronchus. A vascular clamp was placed intrapericardially across the lateral wall of the left atrium incorporating the stumps of the three left pulmonary veins. Care was taken to avoid obstructing the right-sided pulmonary veins with the vascular clamp while still leaving adequate room to fashion the recipient atrial cuff. Each of the three anastomoses was performed with 5-0 Prolene suture (Ethicon, Inc, Somerville, NJ) in continuous fashion. The bronchus was sewn first, followed by the left atrium and then the pulmonary artery. Total operative time for the anastomoses was approximately 30 minutes. Immediately after restoration of ventilation and perfusion to the transplanted left lung, the right pulmonary artery was occluded, thus diverting all cardiac output to the transplanted lung. Survival, arterial oxygen tension, and EVLW were measured at 15 minutes and at 1, 2, 3, and 4 hours.

Measurements of EVLW based on the thermal dye double indicator dilution technique were performed with the Edwards 9310 lung water computer. Ten milliliters of indocyanine dye cooled to 4°C was injected into the central venous catheter. Changes in concentration were then recorded and processed by the microprocessor, which calculated EVLW. Measurements of EVLW were made in triplicate during each study period.

At the conclusion of each experiment, representative sections of the transplanted lung were sampled, fixed with formalin, stained with hematoxylin and eosin, and examined by a pathologist in a blinded fashion.

Statistical Analysis

A univariate repeated-measure analysis of variance was performed to assess group differences and time effects for

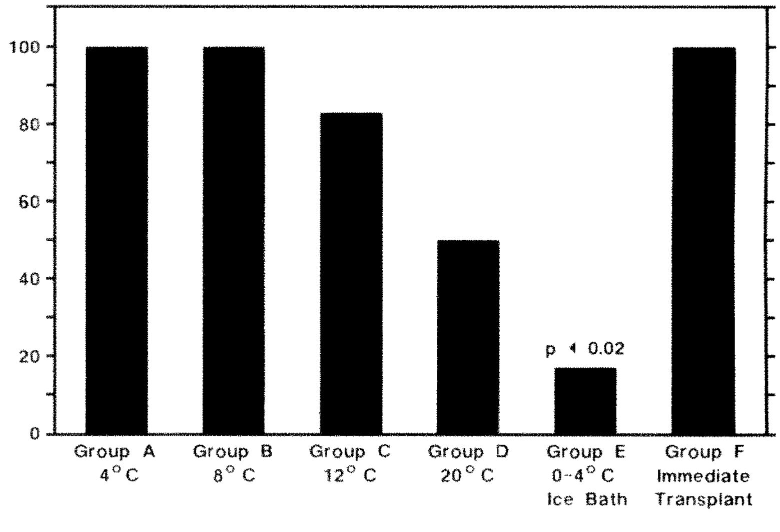

Fig 2. Percent 4-hour survival after unilateral lung transplantation and contralateral hilus occlusion.

Table 1. Arterial Oxygen Tension (kPa) in Transplanted Lung[a]

Time	Group A (4°C)	Group B (8°C)	Group C (12°C)	Group D (20°C)	Group E (0° to 4°C, ice bath)	Group F (immediate transplantation)
15 minutes	45.9 ± 12.5	43.2 ± 20.4	48.4 ± 18.9	32.1 ± 24.5	37.1 ± 13.1	34.4 ± 19.3
1 hour	39.9 ± 13.2	49.7 ± 21.6	48.1 ± 16.9	21.2 ± 10.5[b]	6.4 ± 2.4[b]	42.0 ± 16.3
2 hours	36.4 ± 18.9	42.5 ± 20.9	42.3 ± 19.6	10.1 ± 2.5	ND	35.2 ± 18.0
3 hours	37.2 ± 16.7	41.6 ± 21.1	35.7 ± 16.1	8.5 ± 2.3	ND	34.3 ± 16.5
4 hours	37.5 ± 16.8	29.3 ± 15.6	25.1 ± 15.7	8.3 ± 2.0	ND	31.1 ± 17.1

[a] Measurements are mean ± standard deviation. [b] $p < 0.01$: group E versus group F, group E versus group A, group D versus group A.

ND = not done, because 5 of 6 animals in this group died before the 2-hour measurements could be made.

EVLW and arterial oxygen tension. Holm's simple sequential multiple comparison procedure was used. Fisher's exact test for r × c contingency tables was used to compare the distribution of the proportion of animals surviving in each group. Fisher's exact test was used to test for differences between specific groups.

Results

The 4-hour survival data for each of the six groups are presented in Figure 2. The 100% survival of transplanted animals whose lungs had been stored with cold air at 4°C and 8°C in the Transplanthermm container and of the control animals was significantly greater ($p < 0.02$) than that of animals transplanted with lungs having been stored in an ice-slush bath at 0° to 4°C (17%). Recipients of lungs stored in cold air at 12°C and 20°C experienced 83% and 50% 4-hour survival, respectively.

The effects of different storage techniques on gas exchange are shown in Table 1. After 1 hour of reperfusion to the transplanted lung, the arterial oxygen tension in animals with transplanted lungs that had been stored at 0° to 4°C in an ice-slush bath was significantly ($p = 0.0001$) less than that in animals with transplanted lungs that had been stored at 4°C in the Transplanthermm container and animals with lungs transplanted immediately after harvest. This indicates superior gas exchange in the latter groups.

The quality of lung preservation as indicated by EVLW is presented in Table 2. At 15 minutes and 1 hour after reperfusion to the transplanted lung, EVLW was significantly greater ($p < 0.01$) in lungs stored in an ice-slush bath than in control transplanted animals and in animals transplanted with lungs stored in cold air at 4°C. Lungs stored at 4°C in the Transplanthermm container also had lower EVLW measurements than each of the other experimental groups at each time interval studied, indicating a tendency toward better preservation at 4°C. The p values, however, in this latter comparison were greater than 0.05.

Histological examination of the lung at the conclusion of each experiment revealed moderate to severe intraalveolar edema, interstitial edema, and perivascular cuffing in lungs stored in an ice-slush bath or in the Transplanthermm container at 20°C (Fig 3). In contrast, controls and lungs stored at 4°C and 8°C in the Transplanthermm container had no changes or exhibited only minor changes of intraalveolar edema, interstitial edema, and perivascular cuffing.

Comment

The ability to preserve lungs for longer than 4 hours would have a substantial impact on donor availability for clinical lung transplantation. Studies performed to improve lung preservation can be divided into three specific areas: initial cooling, improved storage, and prevention of reperfusion injury.

The first clinical series of successful lung transplantations used the technique of metabolic inhibition by topical cooling of the lung with cold saline solution, followed by

Table 2. Transplanted Lung Extravascular Lung Water (mL/kg)[a]

Time	Group A (4°C)	Group B (8°C)	Group C (12°C)	Group D (20°C)	Group E (0° to 4°C, ice bath)	Group F (immediate transplantation)
15 minutes	3.76 ± 0.63	6.04 ± 2.39	5.28 ± 1.46	13.18 ± 8.29	15.45 ± 5.63[b]	4.69 ± 1.65
1 hour	4.58 ± 1.17	6.24 ± 2.52	6.32 ± 2.79	12.13 ± 5.89	18.70 ± 7.37[b]	5.33 ± 2.17
2 hours	4.72 ± 1.25	7.18 ± 2.34	7.54 ± 4.59	12.42 ± 3.68	ND	5.63 ± 1.62
3 hours	5.03 ± 1.41	7.77 ± 3.66	7.91 ± 4.62	17.08 ± 7.92	ND	4.89 ± 1.62
4 hours	5.36 ± 1.83	8.63 ± 3.22	9.82 ± 4.87	12.79 ± 3.18	ND	5.89 ± 2.50

[a] Measurements are mean ± standard deviation. [b] $p < 0.01$: group E versus group A, group E versus group F.

ND = not done, because 5 of 6 animals in this group died before the 2-hour measurements could be made.

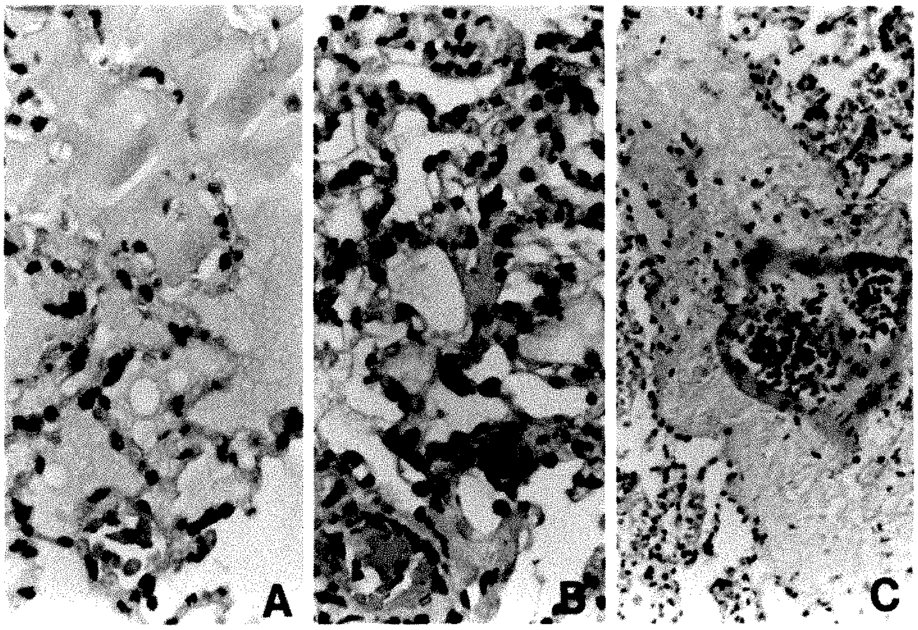

Fig 3. Histological appearance of the lung after 8 hours of storage in an ice-slush bath: (A) intraalveolar edema; (B) interstitial edema; and (C) perivascular cuffing.

hypothermic immersion of the lung in an ice-slush bath during transport [3]. Attempts to enhance the initial cooling of the lung and thereby lengthen preservation times were made with various pulmonary artery flush solutions. Many of these solutions have had beneficial effects on preservation [5–8]. The use of vasodilators in the flush solution has improved the rate and distribution of cooling [11–13], and initial cooling has been enhanced by core cooling with cardiopulmonary bypass. However, both beneficial [14] and less optimal [15] results have been reported.

Lung injury may also occur at the time of reperfusion of blood through the preserved lung. Oxygen free radicals [16, 17], prostaglandin metabolites [18], and calcium influx [19] have all been implicated in the genesis of this injury. Improved lung function after transplantation has also been demonstrated with agents that counteract each of these factors [19–21].

Among the techniques used to improve lung storage, hypothermic immersion of the protected organ in an ice-slush bath has been the most commonly used, both experimentally and clinically [22, 23]. Autoperfusion systems for lung transplantation have been inconsistent and complicated [22, 23]. A chemical method of cooling has been used successfully in England for the storage and transport of donor heart-lung organs [24], and we describe in this study the use of a container that keeps the stored organ cool with cold air at a precise temperature.

Several explanations exist for the superior lung preservation when the lung is stored in cold air at 4°C as opposed to when it is immersed in an ice-slush bath at 0° to 4°C. When the lung is stored in cold air with the bronchus open, cold air may cool through the open bronchus as well as through the pleural surface. In contrast, when the lung is immersed in an ice-slush bath, cooling occurs only across the pleural surface.

The rate of cooling may also play an important role in lung preservation, in that the core temperature of the lung decreases faster when the lung is immersed in an ice-slush bath than when it is placed in the Transplanthermm container at 4°C. Preliminary studies in our laboratory have shown that the rate of lung cooling in cold air is similar to that obtained with pulmonary artery flush solutions (unpublished data).

Another explanation for better lung preservation in cold air is the actual temperature at which the lung is stored. In an ice-slush bath, the core lung temperature has been recorded at temperatures less than 4°C. In contrast, core lung temperatures lower than 4°C have not been recorded with cold air storage. Temperatures lower than 4°C might prove hazardous to the functional integrity of the lung unit while maintaining cell viability, as demonstrated with storage temperatures of −2°C to −5°C by others [25]. Future studies are planned to evaluate the role of each of these variables.

Cold air storage in the Transplanthermm container has several additional advantages: the container is reusable and thus initial costs are soon absorbed; unlike clumsy autoperfusion setups, the container is ready to use and is easily transportable; the temperature to which the lung is exposed can be adjusted by altering the initial temperature of the solution placed in the water jacket; the container is shock-proof, thus preventing mechanical damage to the organs; and organs are shielded from contamination should the seal of the storage bags break. In contrast, organs preserved by hypothermic immersion are at risk to contamination if there is a leak in the storage bags [24]. Also, we anticipate that improved preservation during transport with cold-air storage will act in concert with the techniques that enhance initial cooling and prevent reperfusion injury.

In conclusion, this study demonstrated that traditional hypothermic immersion alone of the lung for 8 hours did not provide adequate preservation for unilateral lung transplantation, whereas storage in cold air for 8 hours at 4°C and 8°C resulted in excellent survival and postoperative performance of the lung. We hope that future studies will show further enhancement of lung preservation by cold air storage when other techniques that maximize benefits to the lung during initial cooling and prevent reperfusion injury are also used.

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References

1. Toronto Lung Transplant Group. Unilateral lung transplantation for pulmonary fibrosis. N Engl J Med 1986;314:1140–5.
2. Patterson GA, Cooper JD, Dark JH, Jones MT, Toronto Lung Transplant Group. Experimental and clinical double lung transplantation. J Thorac Cardiovasc Surg 1988;95:70–4.
3. Toronto Lung Transplant Group. Experience with single-lung transplantation for pulmonary fibrosis. JAMA 1988;259: 2258–62.
4. Fujimura S, Handa M, Kondo T, Ichinose T, Shiraishi Y, Nakada T. Successful 48-hour simple hypothermic preservation of canine lung transplants. Transplant Proc 1987;19: 1334–6.
5. Hachida M, Morton DL. Lung function after prolonged lung preservation. J Thorac Cardiovasc Surg 1989;97:911–9.
6. Paull DE, Keagy BA, Kron EJ, Wilcox BR. Improved lung preservation using a dimethylthiourea flush. J Surg Res 1989;46:333–8.
7. Locke TJ, Hooper TL, Flecknell PA, McGregor CGA. Preservation of the lung. Comparison of topical cooling and cold crystalloid pulmonary perfusion. J Thorac Cardiovasc Surg 1988;96:789–95.
8. Yamazaki F, Yokomise H, Keshavjee SH, et al. The superiority of an extracellular fluid solution over Euro-Collins' solution for pulmonary preservation. Transplantation 1990; 49:690–4.
9. Robicsek F, Masters TN, Duncan GD, Denyer MH, Rise HE, Etchison M. An autoperfused heart-lung-preparation: metabolism and function. Heart Transplant 1985;4:334–8.
10. Wang LS, Yoshikawa K, Miyoshi S, et al. The effect of ischemic time and temperature on lung preservation in a simple ex vivo rabbit model used for functional assessment. J Thorac Cardiovasc Surg 1989;98:333–42.
11. Harjula ALJ, Starkey TD, Hagberg RC, Baldwin JC. Intravenous prostaglandin E1, cold crystalloid flush and topical hypothermia for cardiopulmonary graft preservation. Ann Chir Gynaecol 1987;76:56–60.
12. Jurmann MJ, Dammenhayn L, Schäfers HJ, Wahlers T, Fieguth HG, Haverich A. Prostacyclin as an additive to single crystalloid flush: improved pulmonary preservation in heart-lung transplantation. Transplant Proc 1987;19:4103–4.
13. Lehtola A, Harjula A, Heikkilä L, et al. Single-lung allotransplantation in pigs following donor pretreatment with intravenous prostaglandin E-1. Morphologic changes after preservation and reperfusion. Scand J Thorac Cardiovasc Surg 1989;23:193–9.
14. Pillai R, Fraser C, Bando K, Brawn J, Reitz B, Baumgartner W. Core cooling remains the most effective technique of extended heart-lung (HL) preservation: further experimental evidence. Transplant Proc 1990;22:551–2.
15. Harjula A, Baldwin JC, Shumway NE. Donor deep hypothermia or donor pretreatment with prostaglandin E_1 and single pulmonary artery flush for heart-lung graft preservation: an experimental primate study. Ann Thorac Surg 1988;46:553–5.
16. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 1985;312:159–63.
17. Parks DA, Bulkley GB, Granger DN. Role of oxygen free radicals in shock, ischemia, and organ preservation. Surgery 1983;94:428–32.
18. Demling RH. Role of prostaglandins in acute pulmonary microvascular injury. Ann NY Acad Sci 1982;384:517–34.
19. Hachida M, Morton DL. The protection of ischemic lung with verapamil and hydralazine. J Thorac Cardiovasc Surg 1988; 95:178–83.
20. Detterbeck FC, Keagy BA, Paull DE, Wilcox BR. Oxygen free radical scavengers decrease reperfusion injury in lung transplantation. Ann Thorac Surg 1990;50:204–10.
21. Hachida M, Morton DL. A new solution (UCLA formula) for lung preservation. J Thorac Cardiovasc Surg 1989;97:513–20.
22. Toledo-Pereyra LH, Hau T, Simmons RL, Najarian JS. Lung preservation techniques. Ann Thorac Surg 1977;23:487–94.
23. Egan TM, Kaiser LR, Cooper JD. Lung transplantation. Curr Probl Surg 1989;26:673–752.
24. Wheeldon DR, Wallwork J, Bethune DW, English TAH. Storage and transport of heart and heart-lung donor organs with inflatable cushions and eutectoid cooling. J Heart Transplant 1988;7:265–8.
25. Okaniwa G, Nakada T, Kawakami M, et al. Studies on the preservation of canine lung at subzero temperatures. J Thorac Cardiovasc Surg 1973;65:180–6.

DISCUSSION

DR RICHARD E. CLARK (Pittsburgh, PA): This, I think, will be a major advance if the data are supported. However, I just do not understand the mechanism by which this might work. Did you measure the temperature of the lung tissue itself in the hypothermic immersion system? To have such poor results in the immersion group compared with the air group, one must invoke a cold injury or some other mechanism to explain these very large differences. I would appreciate your thoughts.

DR KON: We do not have any specific data to explain what the mechanism is or why the cold air works better, but we certainly have several thoughts about it. One thing we obviously were concerned about in the ice-slush animals was why survival was so poor. We did study some lungs at just 4 to 6 hours of storage, and, as has been reported in the literature, we had good survival. So, we do not think that the poor survival was directly related to some sort of immediate frostbite-type injury. We also looked histologically at pleural surfaces of the ice-slush preserved lung, and saw no type of injury there either. All the injury was in the lung parenchyma itself, as we have shown on the slides.

So there are several hypotheses as to why the results were better with cold-air storage. The thermal conductivity of water and that of air are obviously different. Cold air cools the lung mainly by convection, whereas ice slush cools the lung mainly by conduction. Therefore, the rate of cooling of the lung was different. We have done subsequent studies on the rate of both cold-air and ice-slush cooling, and have found the rate of cooling with cold air to be more similar to the rate of cooling with a flush solution. That is another reason why the rate of cooling might have played a role. Finally, when the lung sits in the Transplanthermm container with cold air surrounding it, the cold air can enter the open bronchus and possibly directly protect the alveolar membrane, whereas, when the lung is immersed in an ice-slush bath, we think cooling can only occur across the pleural surface. This too, may be related to the improved preservation when cold-air storage is used.

DR FREDERICK L. GROVER (San Antonio, TX): In the group that was submerged, did you staple the bronchus so that fluid could not get into the bronchus?

DR KON: We did not staple the bronchus, but what we did was to bring the plastic bag right outside the top of the styrofoam cooler so water could not get into it. Otherwise immersion would have drowned the lung.

DR GROVER: In the submerged group, did you do any studies to see if there was any absorption by the lung of the fluid in which it was immersed? Could that account for the difference between the two groups?

DR KON: We did not do any studies and have no knowledge that that occurred, either.

Notice From the American Board of Thoracic Surgery Regarding Trainees and Candidates for Certification Who Are Called to Military Service Related to the Persian Gulf Conflict

The Board appreciates the concern of those who have received emergency call to military service. They may be assured that the Board will exercise the same sympathetic consideration as was given to candidates, in recognition of their special contribution to their country, during the Korean and Viet Nam conflicts with regard to deadlines, applications, examinations, and interruption of training.

Harvey W. Bender, Jr, MD
Chairman
The American Board of Thoracic Surgery

Surgical Treatment of the Wolff-Parkinson-White Syndrome by Epicardial Electrical Ablation

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A new operation to eliminate accessory pathways—epicardial electrical ablation—is described. In a group of 201 patients without concomitant disease, the mortality rate was 0.5% and the overall efficacy of the operation for free wall accessory pathways, 98%. A retrospective clinical study of 44 unselected patients was performed to examine how safe epicardial electrical ablation is. The criteria for intraoperative effectiveness were disappearance of both the delta wave and retrograde conduction and inability to induce tachycardia. In the postoperative and follow-up periods, the following were reviewed: electrocardiograms; Holter monitor recordings (24 to 26 hours); release of the myocardial-specific isoenzyme of creatine kinase; intracardiac hemodynamics and myocardial contractility (radionuclide methods); selective coronary arteriograms and ventriculograms; mean work capacity (bicycle ergometer); diagnostic transesophageal electrical stimulation; and histology of the area of ablation. The main conclusion of this study is that epicardial electrical ablation is a highly efficient and safe operation for surgical elimination of parietal accessory pathways in patients with Wolff-Parkinson-White syndrome. Its advantages are its technical simplicity and the opportunity to review results immediately during the operation.

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Several operations are now used for the surgical treatment of Wolff-Parkinson-White (WPW) syndrome. The data from various institutions show that the initial experience is very important [1] and that successful results are achieved in 86% to 99% of patients [1–5]. A success rate of 100% has been reported as well. In the latest series [6], 96% of 215 patients had successful ablation of accessory pathways (APs) using catheter fulguration.

There is no one method for AP elimination that satisfies all surgeons. In fact, considering WPW syndrome as a single disease entity from the surgical point of view, elimination of the pathways is a task with many unknowns. The different locations of the APs change considerably the type of operation and the results. To make it widely used and to increase the rate of success, the operation should be as simple as possible. We [7] have developed the procedure of epicardial electrical ablation (EEA) of the Kent bundle AP, and it satisfies this requirement. In patients without concomitant disease, EEA decreased mortality to 0.5%, and the overall efficacy of the operation for free wall APs was 98%. We believe these results will improve with more experience. The question is, how safe is EEA? The purpose of this report is to present an objective evaluation of the effectiveness of the procedure.

For editorial comment, see page 527.

Material and Methods

A retrospective clinical study was performed in a group of unselected patients. The surgical results and data obtained during the operation, during the early postoperative period, and at later follow-up (to 4 years) were examined.

Patient Population

From March 1980 to June 1, 1989, 305 patients underwent an open heart operation for WPW syndrome. A left free wall AP was present in 151 patients, a right free wall AP in 80, a septal AP in 50, and multiple APs in 24 patients. The function of the AP was manifest in 179 patients, intermittent in 38, latent in 6, concealed in 58, and multiple in 24. Fifty patients underwent the procedure of Sealy and 54, Sealy's procedure combined with a cryoprobe. The other 201 patients underwent EEA. Forty-four of these 201 patients form the basis of our retrospective study.

There were 26 male and 18 female patients ranging in age from 6 to 67 years (mean, 34.3 ± 2.1 years). Twenty-six patients had a persistent form of WPW syndrome, 10 had a transient form, and 8 had a concealed form. A left-sided Kent bundle was found in 28 patients, a right-sided bundle in 5, and a septal bundle in 11 patients. The patients underwent preoperative electrocardiographic and electrophysiological studies.

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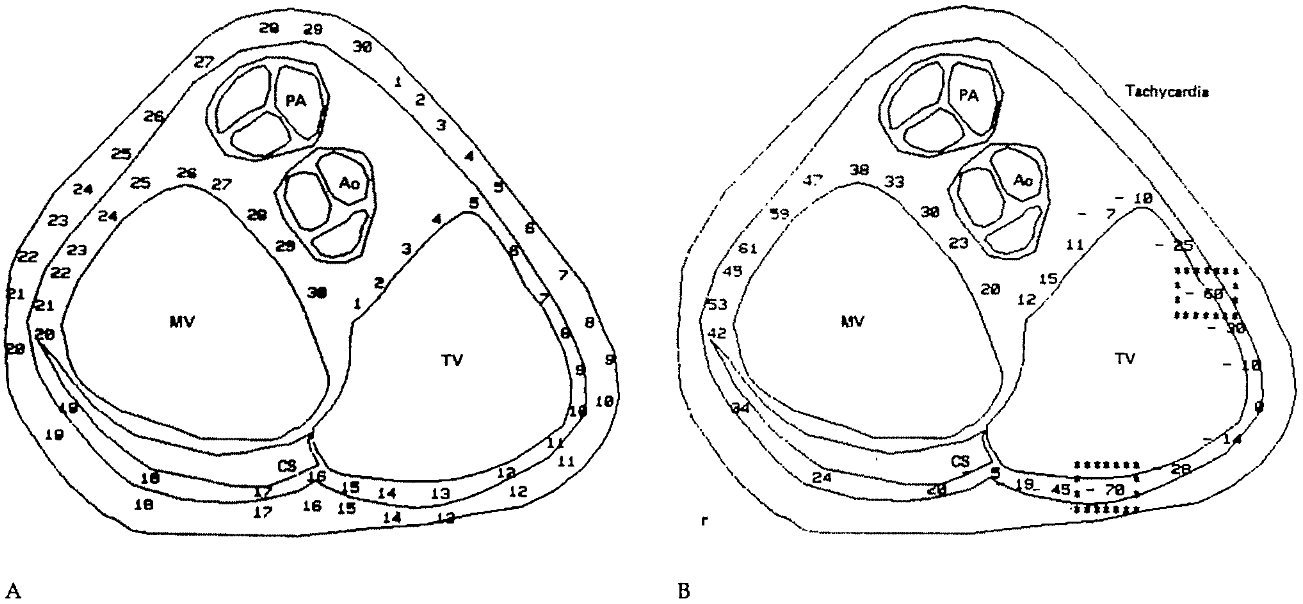


Fig 1. (A) Computer map used for accessory pathway localization during operation. The atrial and ventricular sides of the atrioventricular groove are divided into 30 points. (B) Example of intraoperative diagnosis of two accessory pathways, both right sided (dotted squares). (Ao = *aorta;* CS = *coronary sinus;* MV = *mitral valve;* PA = *pulmonary artery;* TV = *tricuspid valve.)*

Operative Technique

The objective of EEA is to deliver a series of electrocardiographic-synchronized shocks along the atrioventricular (AV) groove in the area of AP manifestation from both the atrial and ventricular sides. The cardiac electrode was connected to the negative output of a direct-current defibrillator (Hellige program 19; Germany). The back paddle (anode) was placed under the patient's scapula. The functional surface area (the diameter of the round tip) of the active cardiac electrode was 5 mm.

The operation was performed with normothermic extracorporeal circulation. After sternotomy and pericardiotomy, the heart was mapped. From the AV groove, the heart was divided into 30 points: 15 on the right side, 14 on the left, and one for the crux (Fig 1A). Mapping of the ventricular side of the AV groove was carried out with atrial stimulation and mapping of the atrial side, when tachycardia was induced. As a result of the mapping, the sites of maximum preexcitation in the ventricles and atria were located (Fig 1B).

Normothermic perfusion was then begun. The venae cavae were snared, and the heart was decompressed. To perform EEA of APs in the right posterior, posteroseptal, and left parietal locations, the heart was lifted with a special hook, the branches of which are covered with isolation material. The mean perfusion pressure was maintained at greater than 55 mm Hg. The ablation tip was brought into contact with the atrial side of the AV groove in the area previously determined to contain the anomalous AP, and a sequence of three to five 50-J shocks was delivered.

A similar procedure was performed on the ventricular side of the AV groove, except that a 150-J shock was delivered on the right ventricle and a 200-J shock on the left ventricle (Fig 2). The total energy of ablating shocks through the anomalous APs averaged 1,100 ± 75 J. The tip was never placed directly over the coronary artery or coronary sinus. It was positioned as close as possible above (atrium) or below (ventricle) the vessel but at least 1 mm away from it.

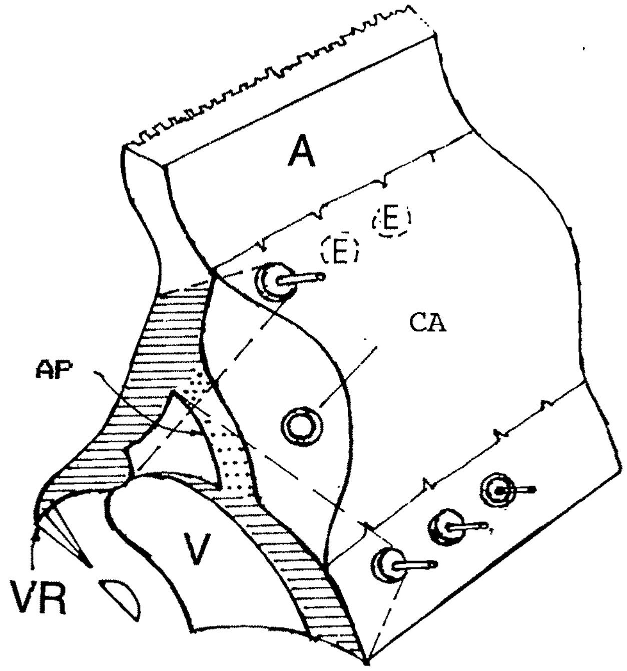


Fig 2. Epicardial electrical ablation of anomalous accessory pathways. (A = atrium; AP = *accessory pathway;* CA = *coronary artery;* E = *site of electrical ablation;* V = *ventricle;* VR = *valve ring;* striped area = *area of electrical ablation.)*

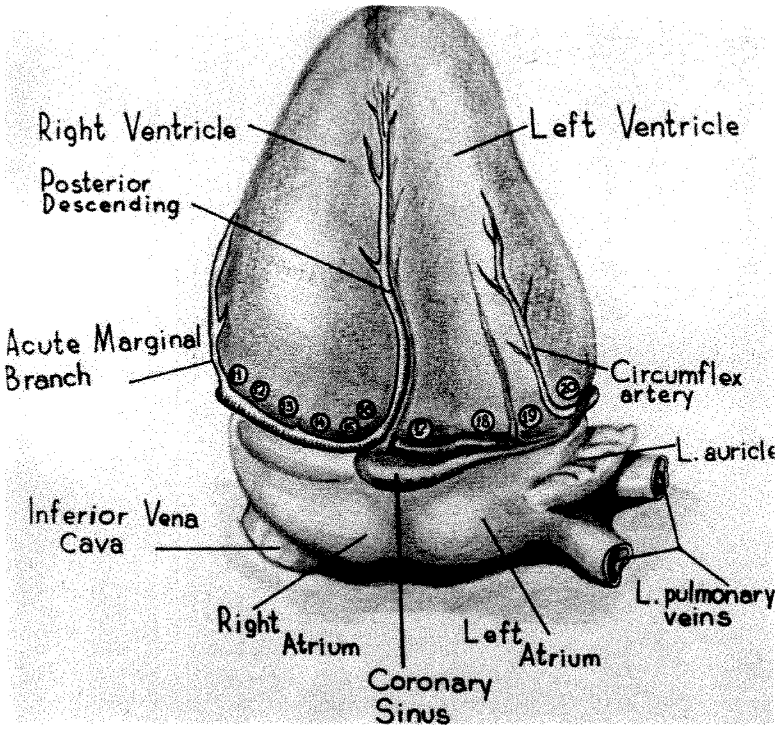


Fig 3. Points of epicardial electrical ablation on ventricular side of atrioventricular groove. Point 19 is the most frequent area of accessory pathway location in patients with a left-sided Kent bundle. For points 17 and 18, when the heart is lifted up, it usually is easy to ablate the accessory pathway between the coronary artery and coronary sinus.

When all ablating shocks had been delivered, electrophysiological testing of the effectiveness of the operation was carried out. The criteria for effectiveness were disappearance of the delta wave on the electrocardiogram (ECG), disappearance of retrograde conduction, and inability to induce tachycardia. When testing was completed, cardiopulmonary bypass (average time, 36.3 ± 2.9 minutes) was discontinued, and the studies were repeated. If satisfactory results were obtained, the operation was terminated in routine fashion.

It should be pointed out that the ablation procedure has been modified continually since it was first performed. We began with the ablation of the atrial side of the AP [7]. That both the atrial and ventricular sides should be electrically shocked was an empirical decision that came later on and did not depend on the results. At present, the cumulative experience is convincing that the side of ablation of the AP (atrial, ventricular, or both) depends totally on which places the AP as close to the electrical tip as possible.

For example, a right free wall AP can be reached easily from the atrial side of the AV groove. Only when ablation is not achieved from that side is the electrical shock from the ventricular side of the AV groove added. In patients with a left-sided AP at point 19 (Fig 3), ablation of the Kent bundle from only the ventricular side might be enough to eliminate the preexcitation. For points 17 and 18, when the heart is lifted up, it is possible to put the ablating tip between the coronary artery and coronary sinus. The shock in this area totally destroys the function of the AP after two to three discharges. For points 20 to 25, both the atrial and ventricular sides of the AV groove should be shocked. In the 44 study patients, the surgical procedure was performed under normothermic extracorporeal circulation from both the atrial and ventricular sides of the AP without attention paid to the location of the Kent bundle.

Evaluation of the Effectiveness of Operation and Myocardial Damage

The effectiveness of the operation and the degree of damage to the myocardium are interrelated. The results obtained in the operating room were evaluated by generally accepted electrophysiological criteria and in the follow-up period, by the absence of attacks of tachycardia. Because the effects of electrical ablation have not been previously studied, there is a question as to what kind of myocardial damage might occur [8].

To answer this question, patients underwent several types of studies. Standard 12-lead ECGs were recorded before operation, twice during the operation (three-lead ECG), every 12 hours for 3 to 4 days postoperatively, before discharge from the hospital, and then every 6 to 12 months. Holter monitoring was performed during the first postoperative day. In addition, release of total creatine kinase (CK) and its MB isoenzyme (CK-MB) was analyzed every 3 to 4 hours after the operation for 4 hours. The total CK was determined by a modification of the kinetic method of Szasz and colleagues [9] by using antiserum to MB subunits.

Electrocardiographic-synchronized radionuclide ventriculography was performed in 19 patients before the operation and 1 month postoperatively in the left anterior oblique projection (30 degrees to 60 degrees) using in vivo erythrocytes labeled with technetium 99. The preparation in the amount of 25 mCi was injected into the cubital vein.

Table 1. Results of Intraoperative and Postoperative Studies in Patients Having Epicardial Electrical Ablation[a]

			Postoperative		
Study	Preop	Intraop	Day 1	1–2 Months	1–4 Years
Electrocardiography (patients)					
ST segment (subepicardial) (n = 25)	0	13	7	0	0
ST segment (subendocardial) (n = 25)	0	11	0	0	0
T wave (negative) (n = 25)	0	1	0	0	0
Q wave (n = 32)	0	0	3	2	0
Biochemistry					
Q CK-MB (Eq) (n = 18)	...	...	5.26 ± 0.9	...	...
Hemodynamics					
Radionuclide studies (n = 19)					
LVEF	0.623 ± 0.019	...	...	0.611 ± 0.012	...
EDV (mL/m^2)	79.7 ± 5.8	...	...	69.3 ± 4.5	...
ESV (mL/m^2)	30.2 ± 3.1	...	...	26.6 ± 1.9	...
SI (mL/m^2)	49.5 ± 3.19	...	...	42.7 ± 2.8	...
Angiography (n = 9)					
LVEF (n = 8)	...	...	...	...	0.58 ± 0.0193
EDV (mL/m^2) (n = 8)	...	...	...	...	88.2 ± 4.38
ESV (mL/m^2)	...	...	...	...	36.9 ± 2.43
SI (mL/m^2)	...	...	...	...	51.3 ± 3.16
Mean work capacity (n = 22)[b]	110 ± 1.8	...	...	96.4 ± 5.4	100 ± 6.9

[a] Where applicable, data are shown as the mean. [b] This was calculated using bicycle ergometer exercise testing, and the data are shown in watts.

EDV = end-diastolic volume; ESV = end-systolic volume; LVEF = left ventricular ejection fraction; Q CK-MB = cumulative activity of myocardial-specific isoenzyme of creatine kinase; SI = stroke index.

Studies were carried out with a Sigma 4105 gamma camera (Ohio Nuclear) and an MC-560 computer. The recording period averaged 7 minutes. The following variables were studied: right ventricular ejection fraction (EF), left ventricular EF, total EF, EF of three segments (septum, apex, and lateral free wall), and EF in the first third of systole. The end-systolic and end-diastolic volumes, percentages, and mean rate of myocardial fiber shortening were also determined.

To evaluate changes in the force of myocardial contraction after electrical ablation, left ventriculography was performed in 8 patients and right ventriculography in 1 patient depending on the location of the Kent bundle. Data obtained from analysis of intraventricular and aortic pressures included aortic systolic pressure, aortic diastolic pressure, mean blood pressure, and the initial and end-diastolic pressures in the left ventricle. Using the ventriculograms of the 9 patients, analysis of regional and total myocardial function of the left and right ventricles was carried out using a coordinate reference system [10] and methods of quantitative estimation of regional myocardial force function with the computer system Volumat compact (Siemens-Elema).

To determine damage to the vessels in the AV groove, coronary arteriography was performed in 9 patients from 1 month to 46 months postoperatively (average time, 16.3 ± 1.9 months).

Histological study was done of the hearts of the 2 patients who died 7 and 50 days postoperatively. One of these patients was operated on for right-sided WPW syndrome and Ebstein's anomaly (EEA, atrial septal defect closure, and tricuspid valve replacement) and died of progressive right ventricular insufficiency. The other patient had left-sided WPW syndrome and ventricular septal defect. She underwent a successful operation (EEA and VSD closure) and was discharged. She died of a noncardiac cause. In both patients, the tachycardia was cured, and the associated pathological condition was reconstructed.

Results

When the patients were examined during the in-hospital period after EEA or during follow-up, no clinical signs of heart damage (heart murmur or cardiac insufficiency) were noted.

Electrocardiographic changes were studied in 32 patients. During the operation (immediately after electrical ablation and at the termination of the procedure), subepicardial damage was found in 13 of 25 patients in three standard and three augmented leads. It was demonstrated by an increase in the ST segment from 1 or 2 mm to 9 mm in leads II, III, and aVF. These changes persisted throughout the operation. Deeper subendocardial damage to the posterior wall of the left ventricle was found in 11 patients. This was evidenced by a decrease in the ST segment (2 to 3 mm on average) in leads II, III, and aVF

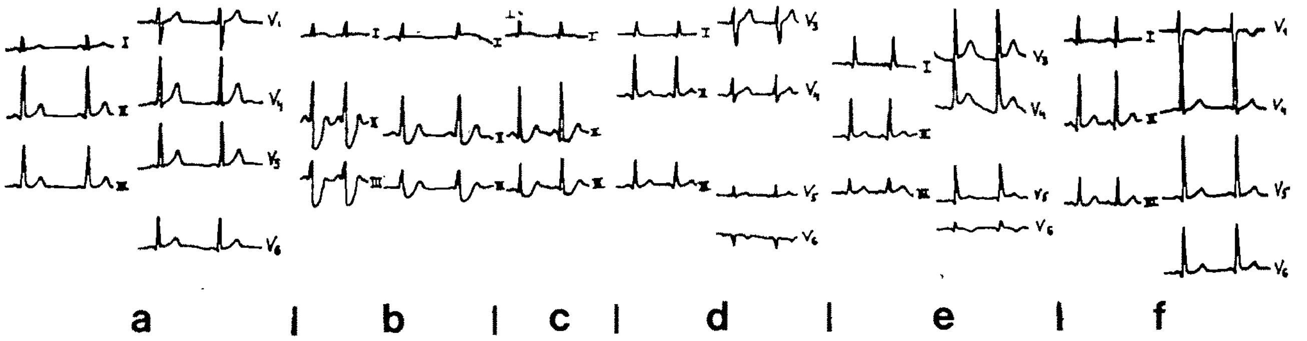


Fig 4. Electrocardiographic dynamics (atypical) in 1 patient: formation and regression of Q wave (a) before and (b) after epicardial electrical ablation and (c–f) on postoperative days 1, 2, 5, and 9, respectively.

and by a reciprocal increase in the ST segment in lead I (Table 1).

By the end of the first postoperative day, these changes (shown by an increase or a decrease in the ST segment) at the site of electrical ablation remained in only 7 of the 32 patients. Ischemia was found in 6 patients (a negative peak T wave), thus indicating that the damage caused by electrical ablation was reversible. Two patients had a disturbance in intraventricular conduction. During the first postoperative day, 3 patients had a pathological Q wave. In 1 of them, subendocardial damage to the posterior wall of the left ventricle was found during the operation as shown by a deep depression of the ST segment (9 mm). The next day, this patient demonstrated infarction of the lateral wall of the left ventricle with the appearance of the pathological Q wave in leads V_6 and V_7 and a decrease in the peak R wave voltage in leads V_5, V_6, and V_7.

On postoperative days 2 through 5, a decrease in the P-Q interval and the appearance of a peak R wave were noted. On postoperative day 9, the pathological Q wave disappeared, and the ECG became normal (Fig 4). Normalization of the ECG indicated very limited damage to the left ventricular lateral wall. Two other patients in whom subepicardial damage occurred during the operation as demonstrated by an increase in the ST segment showed a pathological Q wave and a negative peak T wave on the first postoperative day. The total CK-MB release, however, was much lower than the lower limit seen with a myocardial infarction. This clearly excluded the development of necrosis in these patients.

The ECGs of the remaining patients did not show any abnormalities on the first postoperative day, but 4 of them had some symptoms of early pericarditis. When discharged from the hospital, 2 patients had pathological Q waves. Two additional patients had disturbances in intraventricular conduction. In all other patients, the ECG was normal at the time of discharge.

When the electrocardiographic changes and the operative results were compared, return of tachycardia was not found in any of the patients. However, the delta wave reappeared in 5 of the 11 patients with a septal localization. Subepicardial damage and ischemia of the ablation site were indicated on the ECG on postoperative days 1 through 7. It now seems that the criteria for the efficacy of the operation at the time it is performed are a decrease in the ST segment and a simultaneous disappearance of the delta wave.

In 15 patients, nitroglycerin (0.5 to 2.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was infused before electrical ablation and during the first postoperative day, as it was believed that ablation might induce coronary spasm. Six of these patients had subendocardial damage, 8 had subepicardial damage, and 1 had ischemia of the ablation site. In 2 patients in this group, a new Q wave appeared (2/3 patients with a pathological Q wave). Thus, the efficacy of nitroglycerin was not demonstrated, and we abandoned its use for prophylaxis of myocardial damage.

Studies of the CK-MB levels showed an increased release in all patients. The total output of this isoenzyme varied widely, but the mean value and the deviation from the mean value were not higher than the lower limit of its output established earlier [11].

The release of CK-MB was much higher in patients who had a total energy shock higher than 1,000 J (Fig 5A). A relationship between isoenzyme output and single-shock strength was also found (Fig 5B). However, even when high total energy (more than 1,000 J) and single-shock strength (more than 100 J) were considered together, the average CK-MB level did not reach the lower limit of the infarction level. Our data showed that the myocardial damage appearing with shocks of high energy and strength did not reach even the minimum levels indicative of myocardial necrosis found in patients with small-foci infarctions. In the study group, the degree of myocardial damage was negligible and did not differ from that usually found after cardiac procedures. The relationship of damage to shock strength and energy was indirectly confirmed by the absence of any correlation between duration of extracorporeal circulation and CK-MB levels (Fig 5C).

Intracardiac hemodynamics and myocardial contractility before EEA and in the postoperative period (1 to 2 months) were studied in 19 patients using radionuclide methods (see Table 1). The operation did not cause any changes in end-diastolic or end-systolic volumes. The decrease in left ventricular contractility and the extent and rate of myocardial circular fiber shortening compared with

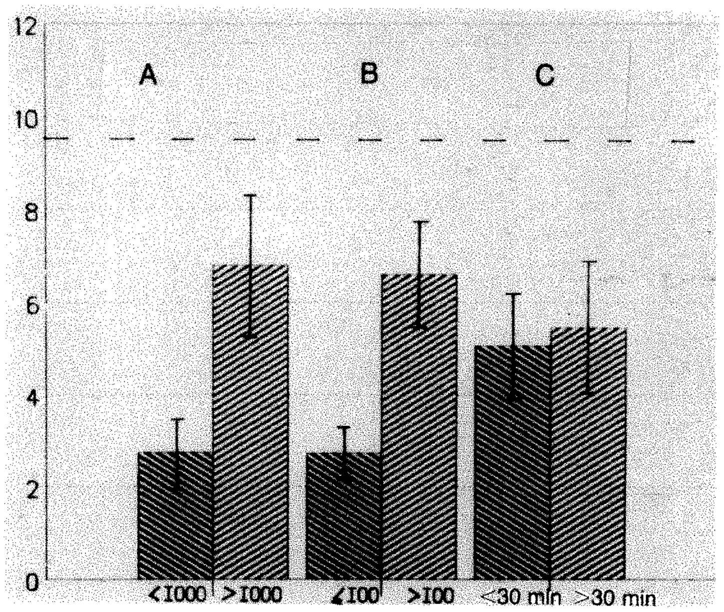


Fig 5. Cumulative activity (Q) of myocardial-specific isoenzyme of creatine kinase and relationship to main variables of electrical ablation and to duration of extracorporeal circulation: (A) Q of creatine kinase-MB when total energy was less than and greater than 1,000 J; (B) Q of creatine kinase-MB when defibrillating shock strength was less than 100 J and from 100 to 200 J; and (C) Q of creatine kinase-MB when the duration of extracorporeal circulation was less than and greater than 30 minutes.

their control values were interesting, but the differences were not significant.

The left ventricular EF before EEA was 0.633 ± 0.019 and after EEA, 0.611 ± 0.012. The right ventricular EF before the operation was 0.387 ± 0.014 and after the operation, 0.41 ± 0.027. Thus, this function was not altered by electrical ablation. Total EF in the postoperative period did not reflect any local changes. The preoperative studies of segmental EFs showed a decrease in the septal EF, but this depended on the localization of the Kent bundle: in patients with WPW syndrome type C (septal localization), the EF was 0.495 ± 0.039 and in patients with type A (left-sided localization), it was 0.622 ± 0.037 ($p < 0.02$). This finding might be explained by the position of an anomalous AP and peculiarities of the excitation propagation in the septum. At the same time, the EFs of the apex and lateral free wall during the preoperative period were within normal limits.

Postoperatively, the septal EF decreased in patients in both groups. In patients with a septal localization of the Kent bundle, the septal EF decreased from 0.495 ± 0.027 to 0.39 ± 0.042. Simultaneously, the EFs of the apex and the lateral free wall of the left ventricle increased. With ablation of a septal Kent bundle, the apical EF increased from 0.62 ± 0.045 to 0.73 ± 0.037, and the lateral free wall EF increased from 0.61 ± 0.051 to 0.73 ± 0.0118. The corresponding results with ablation of a Kent bundle in the free wall were as follows: apical EF before and after EEA, 0.663 ± 0.027 and 0.755 ± 0.014, respectively, and lateral free wall EF, 0.648 ± 0.030 and 0.675 ± 0.025, respectively. Thus, after ablation of a left-sided Kent bundle, the EF of the apical region was more appreciably increased, whereas after ablation of a septal AP, EF increases in the apical region and in the lateral free wall were practically the same.

Thus, the data from the radionuclide studies in the early postoperative period indicate that electrical ablation of the Kent bundle did not cause any changes in intracardiac hemodynamics or in the overall contractile capacity of the ventricular myocardium. It is obvious that with electrical ablation, only a negligible portion of myocardial mass was excluded from the process of contractility, and the procedure did not affect total capacity. Postoperative normalization of the sequence of contraction and an increase in myocardial force of contraction completely compensated for the negligible decrease in segmental contraction and appreciably improved overall myocardial function. This was also confirmed by the clinical course of these 19 patients in the early postoperative period. No instances of cardiac insufficiency were observed, and no deaths occurred.

Selective coronary arteriography and ventriculography were performed in 9 patients 1 to 4 years postoperatively to study long-term results of EEA of APs. A right dominant blood supply was found in 5 patients, a left dominant supply in 3, and a balanced coronary circulation in 1 patient. No damage to the coronary arteries was noted in any of the 9 patients studied (Fig 6).

The data from catheterization did not differ significantly from the data obtained by radionuclide ventriculography and did not show any disturbance in intraventricular hemodynamics. The end-diastolic pressure in most patients was within normal limits and averaged 12 ± 1.1 mm Hg. The end-diastolic volume of the left ventricle was within normal limits (88.2 ± 38 mL/m^2) in all 8 patients studied after a left-sided Kent bundle had been ablated. The end-systolic volume was slightly increased (36.9 ± 2.43 mL/m^2). The stroke index varied insignificantly (average value, 51.3 ± 3.16 mL/m^2). The left ventricular EF after electrical ablation of a left-sided Kent bundle was 0.58 ± 0.0193, and in 1 patient who had undergone electrical ablation of a right-sided AP, it was 0.61 (see Table 1).

Analysis of left ventricular contractile function was

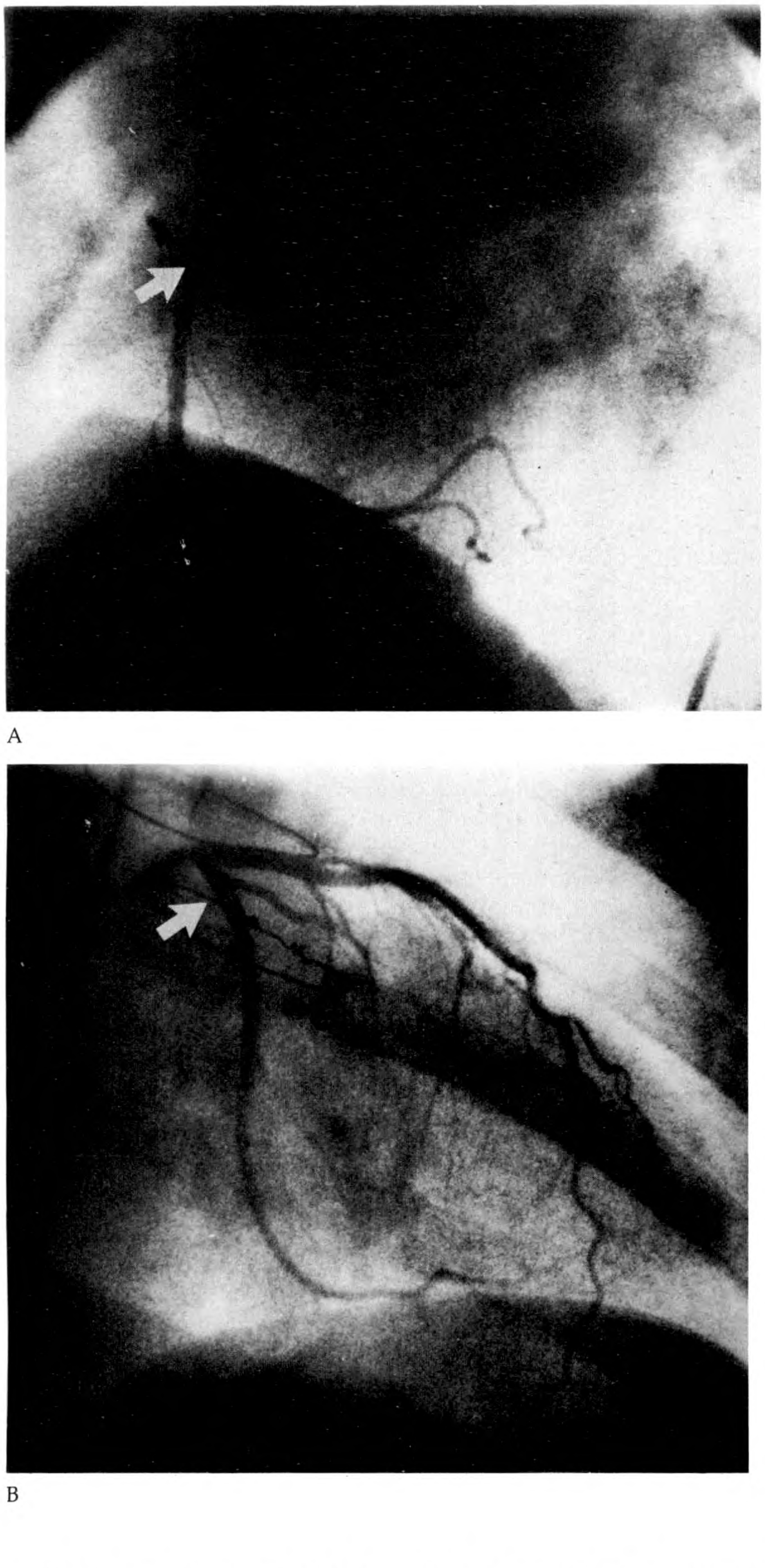


Fig 6. Selective coronary arteriography late postoperatively. Complete patency of (A) the right coronary artery in a 35-year-old patient 42 months postoperatively and (B) the left coronary artery in a 39-year-old patient 37 months postoperatively is preserved in the area of epicardial electrical ablation (arrow). *(*CA = *circumflex artery;* LAD = *left anterior descending coronary artery.)*

carried out in segments to determine the function of different regions of the myocardium after electrical ablation of a left-sided Kent bundle. The sites of dysfunction were found in the area of myocardial ablation and were demonstrated by the decrease in segmental EFs and in the percentage of radial contraction of a given site, localizing within the region from 270 degrees to 350 degrees (segments 9 and 10) in the left anterior oblique projection (Fig 7). In spite of local decreases, the total EF of all patients was within normal limits, a result of both the relatively small mass of damaged myocardium and the increased activity of the other myocardial regions to compensate for

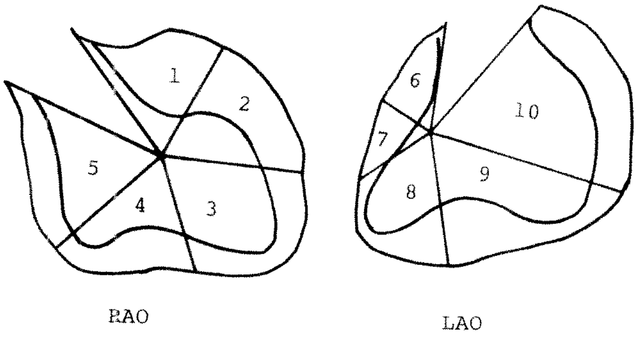


Fig 7. Left ventriculogram made 2 years after operation. Division of ventriculogram into segments is shown in two standard projections, right anterior oblique (RAO) and left anterior oblique (LAO). Site dysfunction is seen in segments 4 and 9 of the left ventricle and partially extends into posterior basal segments 5 and 10.

the deficits of segmental contractility (Fig 8). Confirmation was obtained by measurements of the extent of segmental dysfunction, which occupied not more than 10% to 20% of the area within the angle from 260 degrees to 310 degrees in the left anterior oblique projection.

Tolerance to physical activity was studied in 22 patients preoperatively and 1 to 2 months and 1 to 4 years postoperatively. Mean work capacity was investigated using bicycle ergometer exercise testing. Capacity was slightly decreased 1 to 2 months after the operation, but this was not significant. One to 4 years after the operation, it was normalized (see Table 1).

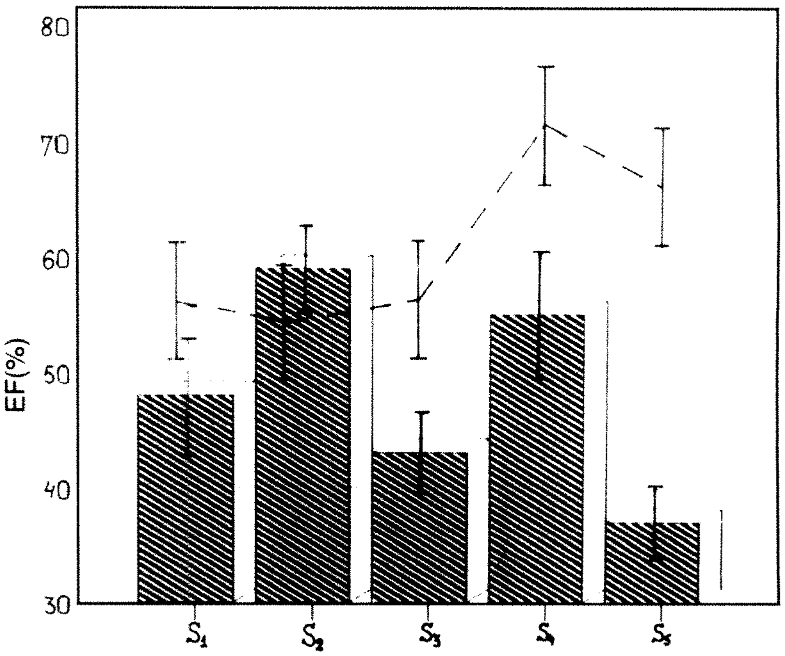
Diagnostic transesophageal electrical stimulation was performed during follow-up (range, 6 to 48 months; mean, 22 ± 4.6 months). During overdrive pacing, high-rate pacing, high-frequency stimulation, and programmed electrical stimulation of the left atrium, the signs of preexcitation and the delta wave were not found. The anterograde effective refractory period of the AV node was 272 ± 9.2 ms. There was a functional right bundle-branch block in 2 patients. An echo zone from 300 to 270 ms with unstable atrial fibrillation or atrial flutter was seen in 2 other patients when a relative refractory period was achieved. The unstable atrial fibrillation or flutter stopped spontaneously, and QRS complexes were narrow. The latter was a sign of anterograde conduction through the AV node–His bundle–Purkinje system.

Evaluation of sinus node function showed normal values when the effect of pacing was studied. Sinus node recovery time after overdrive suppression was 976 ± 46.2 ms. Only in 1 patient with a left free wall Kent bundle were very rare left ventricular extrasystoles registered after overdrive stimulation. They disappeared spontaneously 5 minutes after the pacing was stopped.

Total disappearance of retrograde ventriculoatrial conduction was seen in patients with concealed and intermittent WPW syndrome. Neither an echo zone nor even a single echo beat, the most important criteria of AP ablation, was present.

Histological study of the EEA area showed local contractions with granular, lumpy disintegration 7 days after the procedure. Fifty days after the operation, there was round-cell infiltration in the area of EEA in the left atrium. The necrosis was transmural. There was a fresh connective-tissue scar in the area of ablation, which substituted for myocardium in several places. Local eosinophilic and basophilic infiltration (calcium deposits) was seen in the area of EEA in the left ventricular myocardium. The coronary vessels were completely patent and intact. Media necrosis was found in small-caliber arterial vessels. Based on the histological findings, EEA caused myocardial necrosis and scar tissue formation, the location of

Fig 8. Segmental ejection fraction (EF) of left ventricle after operation. The dotted line shows normal segment (S) function of the left ventricle. Here, the dysfunction is most pronounced in the area of ablation (segments 4 and 5). Compensatory increased function is present along segment 2.



which was strictly restricted by the area of fulguration. It should be emphasized that the changes in the atrium 50 days after EEA were characterized by transmural damage, whereas the changes in the myocardium of the ventricle were local, and the necrotic process extended to separate cells or groups of cardiac cells.

Comment

The detailed analysis of the effectiveness of an operation is of extreme importance for the further development of new areas of surgical intervention. When evaluating the surgical results in patients with WPW syndrome, the main concern of physicians and researchers is the percentage of patients in whom the Kent bundle is ablated. Excellent results were achieved by Cox [12] using the endocardial approach for the surgical division of AV accessory connections; 148 of 149 APs were divided successfully in 118 consecutive patients. The reoperation rate was 0% as was the recurrence rate during follow-up. Cox improved the procedure, and the improvement led to the complete prevention of recurrence of the tachycardia.

There has also been considerable interest in cryoblation for eliminating the Kent bundle. This technique has been used in our country [2] and in Canada [13]. However, an analysis of the long-term postoperative results of these operations has not yet been published.

The operation performed by Sealy and colleagues [8] necessitates the use of extracorporeal circulation with cardioplegia, and experience with the procedure is of great importance. In particular, the operation is a delicate one for the left-sided and the septal location. As a rule, the hearts in these patients are of normal size. Thus, the approach through the interatrial groove to the mitral valve area, along the circumference of which the Kent bundle is ablated, is very limited. In such hearts, extreme skill is required. The use of cardioplegia leads to disturbances in cardiac rhythm early after the restoration of cardiac function. Frequently it makes adequate evaluation more difficult and may cause a delay of some hours in recovery of Kent bundle function.

Epicardial electrical ablation of the Kent bundle as developed at the Bakoulev Institute of Cardiovascular Surgery has none of these drawbacks. The operation is performed through the epicardial approach, which is logical at least for a left-sided AP, as the Kent bundle is located in the epicardium [14]. Cardiac size is of no concern to the surgeon. On the contrary, the smaller the heart, the easier the operation. Most importantly, EEA permits evaluation of the effectiveness of the Kent bundle ablation by the disappearance of the delta wave, by the halt in retrograde conduction, and by the prevention of induced tachycardia immediately after ablation while the patient is still on bypass. This also allows the finding and ablating of a previously unrecognized bundle or bundles.

Undoubtedly, an electric shock applied to the epicardium causes some changes in the ECG. It is reasonable to compare these changes with those observed consequent to a myocardial infarction. Morphological characteristics of ischemic change are seen on the ECG after ablation. However, appropriate analysis shows that these changes are of a different nature. In spite of the fact that changes on the ECG are characterized by a more considerable shift of the ST segment than those observed with a transmural infarction, they are transient, and normalization is observed shortly after operation. The dynamics of the CK-MB level also indicate that these changes are not of an irreversible nature. The values observed are not higher than those usually seen in operations with extracorporeal circulation. That myocardial perfusion is not impaired is shown by the fact that the coronary arteries remain patent, and this is very important for the future of the operation [8]. Intracardiac hemodynamics are not changed. Only segmental decreases in function in the region of the Kent bundle are observed. However, these changes are also found before ablation, as this region is the area of earliest excitation of the ventricles.

The results of our analysis indicate that EEA of a free wall Kent bundle in WPW syndrome provides good immediate and long-term results and does not cause lasting changes in the myocardium; myocardial function is well preserved. However, the delta wave reappeared in 5 of 11 patients with a septal Kent bundle. Though tachycardia did not recur in those patients and the WPW syndrome changed by the WPW phenomena, we did not consider the results of the operation truly positive. That is why patients with septal pathways should have operation by the endocardial approach [15].

Conclusions

1. Epicardial electrical ablation of APs is a highly efficient operation for the surgical management of WPW syndrome. Its advantages are its technical simplicity and the opportunity to immediately evaluate the results of ablation of the Kent bundle during the operation.
2. Myocardial damage caused by electrical ablation of the area of the Kent bundle is transient. The amount of damage is minimal and does not involve coronary vessels or impair cardiac function.
3. The operation is recommended for anomalous APs with a free wall location. For septal pathways, the endocardial approach is still preferable.

References

1. Cox JL, Gallagher JJ, Cain F. Experience with 118 consecutive patients undergoing operation for the Wolff-Parkinson-White syndrome. J Thorac Cardiovasc Surg 1985;90:490–501.
2. Bredikis J, Bukauskas F, Zebrauskas R, et al. Cryosurgical ablation of right parietal and septal accessory atrioventricular connections without the use of extracorporeal circulation: a new surgical treatment. J Thorac Cardiovasc Surg 1985;90:206–11.
3. Guiraudon GM, Klein GJ, Sharma AD, Milstein S, McLellan DG. Closed-heart technique for Wolff-Parkinson-White syndrome: further experience and potential limitations. Ann Thorac Surg 1986;42:651–7.
4. Iwa T, Mukai K, Misaki T, Mitsui T, Matsunaga Y. Surgical management of the Wolff-Parkinson-White syndrome. In: Iwa T, Fontaine G, eds. Cardiac arrhythmias: recent progress

in investigation and management. New York: Elsevier, 1988: 239–50.

5. Penn O. Surgical treatment of the Wolff-Parkinson-White syndrome. Current indications, technique and results. In: Brugada P, Wellens HJJ, eds. Cardiac arrhythmias. Where to go from here? Mt. Kisco, NY: Futura, 1987;573–89.
6. Warin YF, Haissaguerre M. Electrical catheter ablation of accessory pathways. Technique and results in 215 patients [Abstract N550]. Presented at the 7th International Congress Cardiostim 90. Nice, France, June 20–23, 1990:143.
7. Bockeria LA, Mikhailin SI, Revishvili AS, Baturkin LJ, Rybalov AG. Epicardial electric shock ablation of accessory pathways in preexcitation syndrome. In: Fontaine G, Scheinman M, eds. Ablation in cardiac arrhythmias. Mt. Kisco, NY: Futura, 1987:467–78.
8. Gallagher JJ, Selle JG, Svensen RH, et al. Surgical treatment of arrhythmias. Am J Cardiol 1988;1:27A–44A.
9. Szasz G, Grubes W, Betut L. Creatine kinase in serum determination of optimum reaction conditions. Clin Chem 1976;22:650–6.
10. Bockeria LA, Chigogidze NA, Goluchova EZ, Artukhina TV. Total and regional right ventricular activity in idiopathic ventricular arrhythmias. Cardiologia (Russ) 1989;5:30–5.
11. Saprigin DB. Diagnosis and quantitative evaluation of irreversible myocardial lesions through calculation of the cumulative activity of the isoenzyme MB creatine kinase in patients operated on the heart. Cardiologia (Russ) 1982;3:90–7.
12. Cox JL. Surgery for the treatment of refractory tachyarrhythmias. I. Supraventricular tachyarrhythmias. In: Iwa T, Fontaine G, eds. Cardiac arrhythmias: recent progress in investigation and management. New York: Elsevier, 1988:233–7.
13. Guiraudon GM, Klein GJ, Sharma AD, Jones DL, McLellan DG. Surgery for Wolff-Parkinson-White syndrome: further experience with an epicardial approach. Circulation 1986;74: 525–9.
14. Anderson RA, Ho SY, Becker AE. Gross anatomy and microscope of the conducting system. In: Mandel WJ, ed. Cardiac arrhythmias. Their mechanisms, diagnosis and management. 2nd ed. Philadelphia, 1987:13–53.
15. Sealy WC, Wallace AJ, Ramming KP, Gallagher JJ, Svenson RH. An improved operation for the definitive treatment of the Wolff-Parkinson-White syndrome. Ann Thorac Surg 1974;17:107–13.

REVIEW OF RECENT BOOKS

Heart and Heart-Lung Transplantation
By William A. Baumgartner, Bruce A. Reitz, and S. C. Achuff
Philadelphia, W.B. Saunders, 1989
406 pp, illustrated, $140.00

Reviewed by Jolene M. Kriett, MD

This book, similar to a number of other recently published texts, details the basics of heart, combined heart-lung, and lung transplantation including economic aspects, operative techniques, pretransplantation and posttransplantation patient care, immunosuppression, and complications. The majority of the 32 chapters deal with heart transplantation. Although thoroughly covering the major aspects of heart transplantation, many chapters contain somewhat redundant material. For example, immunosuppressive agents and transplant-associated complications are included with similar information in several different chapters. However, for those interested in an overview of many of the basic concerns and techniques in heart and pulmonary transplantation, this text provides an easily readable and concise source of information.

San Diego, California

Membrane Oxygenator Prevents Lung Reperfusion Injury in Canine Cardiopulmonary Bypass

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The effect of blood activation on lung reperfusion injury during cardiopulmonary bypass was investigated in 20 dogs with the use of a bubble oxygenator (n = 10) or a membrane oxygenator (n = 10). In the bubble oxygenator group, significant leukocyte and platelet right to left atrium gradients were found 15 minutes after lung reperfusion ($p < 0.05$, $p < 0.01$) accompanied by a sharp increase in plasma malondialdehyde concentration 5 minutes after lung reperfusion, whereas no significant right to left atrium gradient of leukocytes or platelets nor significant increase in plasma malondialdehyde concentration was observed in the membrane oxygenator group. In both the bubble oxygenator and membrane oxygenator group, similar mild to moderate lung histological changes were found before lung reperfusion. After lung reperfusion, however, more endothelial cell swelling ($p < 0.05$), leukocyte ($p < 0.01$) and platelet ($p < 0.01$) accumulation in lung capillaries, leakage of erythrocytes into the alveolar space ($p < 0.05$), and type I cell damage ($p < 0.05$) were found only in the bubble oxygenator group. Eventually, a significantly higher lung water content was found in the bubble oxygenator group than in the membrane oxygenator group ($p < 0.01$) after cardiopulmonary bypass. This study indicated that lung injury during cardiopulmonary bypass starts mainly after lung reperfusion, which was correlated with lung leukocyte and platelet sequestration associated with different types of oxygenators.

(Ann Thorac Surg 1991;51:573–8)

Lung injury during cardiopulmonary bypass (CPB) is of renewed interest now that complement activation is considered a main mediator leading to lung injury during CPB [1–3]. The complement factor C5a generated by activation of the alternative pathway activates leukocytes that will be sequestrated in the lung microvasculature resulting in lung injury by the released oxygen free radicals, lysosomal enzymes, and arachidonic acid metabolites [4–7]. In addition, platelets are also activated and accumulated in the lungs, which will further contribute to lung injury during CPB [8–10]. Furthermore, the extent of blood activation during CPB is considered to be dependent on the use of a bubble oxygenator (BO) or a membrane oxygenator (MO) [11–13]. However, in clinical situations, studies on lung injury are limited because lung biopsies are needed to analyze lung histological changes during and after CPB.

For editorial comment, see page 529.

The purpose of this experimental study was to evaluate the differences between bubble and membrane oxygenators in regard to the effect on circulating leukocytes and platelets and the associated effect on lung histological changes before and after lung reperfusion in canine CPB.

Materials and Methods

Twenty mongrel dogs weighing 15 to 22 kg were subjected to CPB. All of them received humane care. The dogs were randomly assigned to one of two groups undergoing CPB with a bubble oxygenator containing Dacron material and nylon mesh or a hollow-fiber membrane oxygenator containing polypropylene and polycarbonate materials. All animals underwent a median sternotomy for the establishment of CPB. Both right femoral artery and vein were cannulated for monitoring the mean arterial pressure and the central venous pressure. After the chest was opened, a catheter was inserted into the left atrium for blood sampling. Then anticoagulation was obtained with heparin (300 IU/kg).

The extracorporeal circuit was primed with Ringer's lactate solution. The priming volume with a bubble oxygenator (Canton Type I, Guangzhou, China) was 700 mL, and with a hollow-fiber membrane oxygenator (AL -II, Fu Dan University, Shanghai, China), 800 mL. A roller pump (Shanghai Type III, Shanghai, China) was used in all animals and a Dacron filter with a pore size of 100 μm was incorporated in the arterial line. Cardiopulmonary bypass was achieved by withdrawing the venous blood from cannulas in both the superior and inferior venae cavae through the right atrium, which was returned through a cannula inserted into the left subclavian artery. The ascending aorta was isolated and cross-clamped about 10 minutes after the initiation of CPB. At the same time, both superior and inferior venae cavae were snared around the

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cannulas and total bypass was started. During the aortic cross-clamp period, animals were cooled down to about 25° to 28°C. The CPB time was fixed at 120 minutes and the aortic cross-clamping time was fixed at 90 minutes. No blood or blood products were transfused throughout the whole experimental period. Thirty minutes after CPB, the dogs were killed to obtain lung tissue for histology and determination of lung water content.

Hematology

Blood samples were taken after heparinization, 5 minutes after start of CPB, 5 minutes before, 5 and 15 minutes after release of the aortic cross-clamp, and 30 minutes after CPB from both left and right atrium simultaneously. During the cross-clamping period, blood samples were taken from the outlet of the oxygenator and from the inferior vena cava. Leukocytes and platelets were counted with a cell counter (Coulter Co, Dunstable, UK). Plasma malondialdehyde (MDA) concentration was determined by the measurement of thiobarbituric acid–reactive substances in plasma obtained from heparinized blood representing oxygen free radical release [4]. Each value of blood tests after the initiation of CPB was corrected for hemodilution by hematocrit according to the following formula: corrected value = (sample value × initial hematocrit)/sample hematocrit.

Lung Histology

Lung tissue biopsy specimens were obtained from the upper lobe of the right lung before release of the aortic cross-clamp and 30 minutes after termination of CPB. The specimens were put immediately into 2% glutaraldehyde solution and stored at 4°C for later histological determination, which was performed blindly under an electron microscope (H-500 microscope, Hitachi, Tokyo, Japan) with magnifications of 2,000 to 10,000 times. Three spheres from different parts of each specimen were examined. Pathological changes in the lung tissue were graded as mild (+), moderate (++), and severe (+++) as expressed by endothelial cell swelling, erythrocyte clumping, leukocytes and platelets accumulated within the capillaries, leakage of erythrocytes to the extravascular space, leukocyte migration, and plasma leakage to the alveolar space as well as changes of lung type I and type II cells.

Lung Water Content

The right lung was clamped immediately when the dog was killed 30 minutes after CPB. Two pieces of peripheral lung tissue of 1 cm^3 each that contained no visible bronchial tissue were collected and weighed (Sartorius AG, Goettingen, Germany) to obtain the wet weight. After being put in an oven at about 100°C for 24 hours, the tissue was weighed again to obtain the dry weight. Lung water content was then calculated according to the following formula: lung water content = [(wet weight − dry weight) / wet weight] × 100%.

Statistics

Paired *t* test was used to compare all the hematological data from different sampling times and between left and right atrium, and unpaired Student's *t* test was used to compare the data between BO and MO groups. Spearman's correlation coefficient was used to determine the correlation between lung histological findings and leukocyte or platelet right to left atrium gradient (RA–LA gradient) after release of the aortic cross-clamp. A calculative method of exact probability of contingency [14] was used to determine the differences of pathological changes between lung biopsies before and after lung reperfusion and between BO and MO groups. A *p* value less than 5% was considered statistically significant. Values are expressed as mean and standard error of the mean.

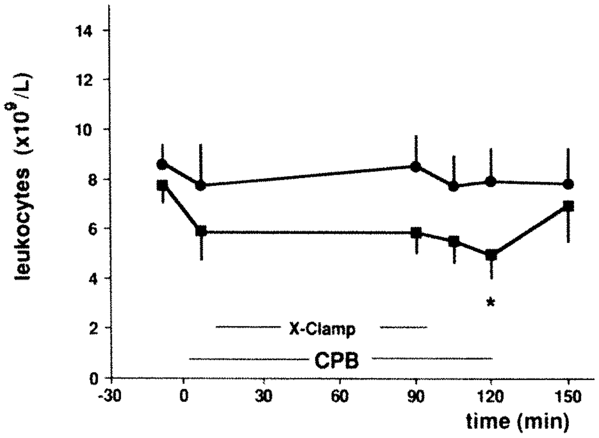

Fig 1. Leukocytes during canine cardiopulmonary bypass (CPB) *in both the bubble oxygenator* (squares) *and membrane oxygenator* (circles) *groups in blood samples obtained from the left atrium. There is a significant decrease in the counts 15 minutes after release of aortic cross-clamp* (X-Clamp) *only in the bubble oxygenator group* (*p < *0.05, paired* t *test with time point of 90 minutes).*

Results

Leukocytes

In the BO group, leukocyte counts decreased 5 minutes after the start of CPB and remained low during CPB, whereas the counts remained high during CPB in the MO group although a slight decrease was also found initially. A significant decrease in leukocyte counts was found 15 minutes after release of the aortic cross-clamp as compared with the counts before the clamp release in the BO group ($p < 0.05$) but not in the MO group in blood samples obtained from the left atrium (Fig 1).

Platelets

An initial decrease in platelet counts was found in both BO and MO groups 5 minutes after the start of CPB (although less severe in the MO group) as compared with the respective baseline value. A further drop was found in the BO group but not in the MO group 15 minutes after release of the aortic cross-clamp ($p < 0.05$) in blood samples from the left atrium (Fig 2).

Plasma Malondialdehyde

The plasma MDA concentration was gradually increased after the start of CPB in the BO group until release of the

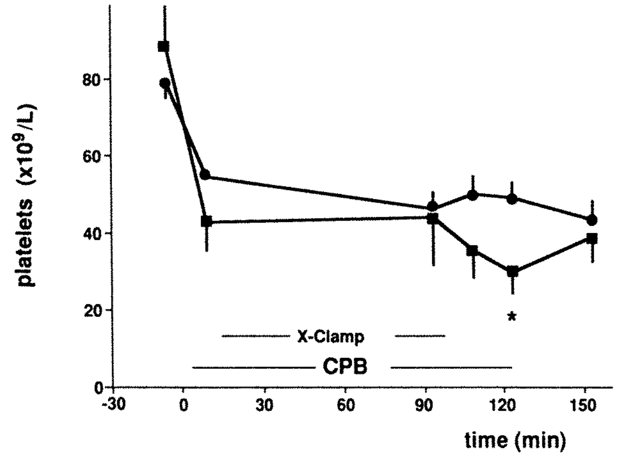

Fig 2. Platelets during canine cardiopulmonary bypass (CPB) *in both the bubble oxygenator* (squares) *and membrane oxygenator* (circles) *groups in blood samples from the left atrium. A significant decrease in platelets was found in the bubble oxygenator group but not in the membrane oxygenator group 15 minutes after cross-clamp* (X-Clamp) *release.*

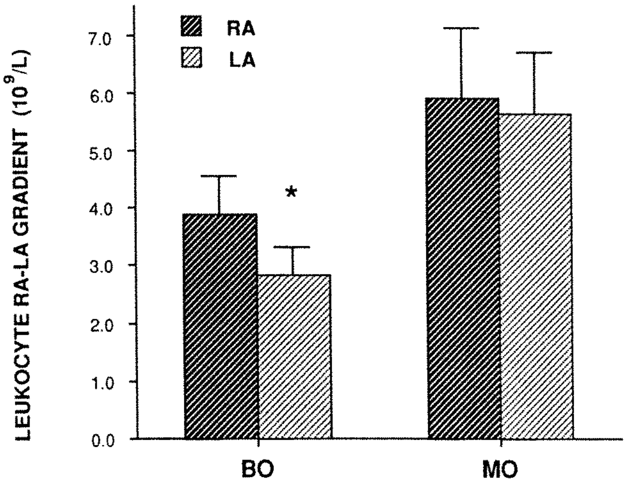

Fig 4. Significant right to left atrium (RA–LA) *gradient of leukocytes* (*$p < 0.05$) *was found in the bubble oxygenator* (BO) *group but not in the membrane oxygenator* (MO) *group 15 minutes after lung reperfusion.*

aortic cross-clamp (from 2.33 ± 0.12 nmol/mL to 6.10 ± 1.33 nmol/mL; $p < 0.05$). Thereafter, MDA concentration increased further to a peak value 5 minutes after lung reperfusion (7.66 + 1.51 nmol/mL; $p < 0.01$) in blood samples from the right atrium. In contrast, the plasma MDA concentration did not increase significantly in the MO group. Thus there was significantly more plasma MDA observed in the BO group than in the MO group ($p < 0.05$) 5 minutes after lung reperfusion (Fig 3).

Sequestration

After 15 minutes' reperfusion of the lungs, leukocyte and platelet counts in the BO group were significantly lower in the samples obtained from the left atrium than in samples from the right atrium (RA–LA gradient; $p < 0.05$ and $p < 0.01$, respectively), whereas no significant differences in leukocyte and platelet RA–LA gradient were found in the MO group (Figs 4, 5).

Lung Histology

In both the BO and MO groups, similar mild to moderate lung histological changes were found before lung reperfusion (Table 1). After lung reperfusion, significant histological changes occurred particularly in the BO group characterized by more leukocyte ($p < 0.01$) and platelet ($p < 0.01$) accumulation in the lung capillaries, more endothelial cell swelling ($p < 0.05$), more leakage of erythrocytes into the alveolar space ($p < 0.05$), and more damage

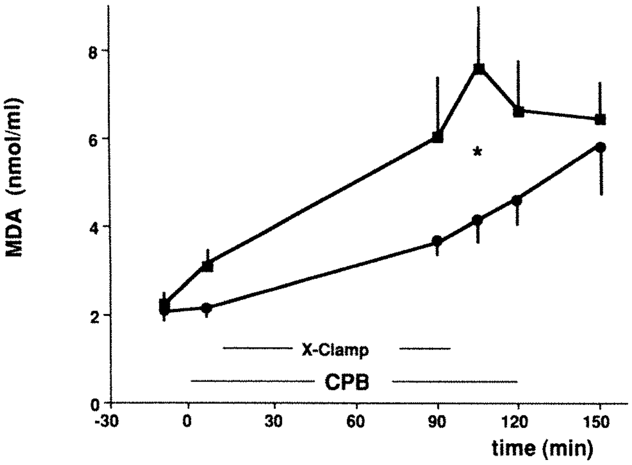

Fig 3. The plasma malondialdehyde (MDA) *level increased gradually after the initiation of cardiopulmonary bypass* (CPB) *in the bubble oxygenator group* (squares) *and increased further 5 minutes after release of the cross-clamp* (X-Clamp) *with a significant higher level* (*$p < 0.05$) *than that in the membrane oxygenator group* (circles).

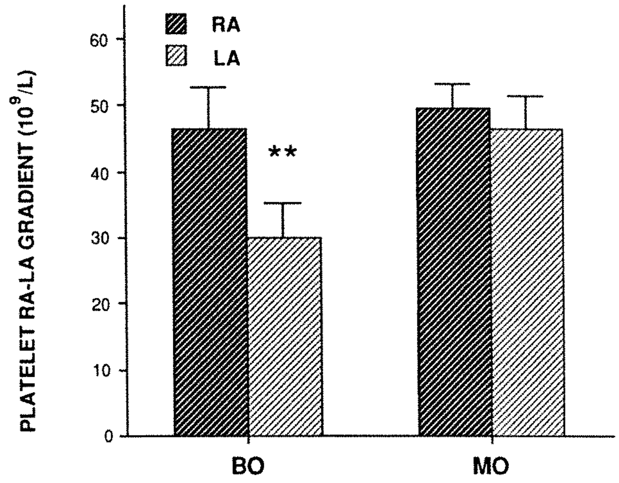

Fig 5. Significant right to left atrium (RA–LA) *gradient of platelet numbers* (**$p < 0.01$) *was found in the bubble oxygenator* (BO) *group but not in the membrane oxygenator* (MO) *group 15 minutes after lung reperfusion.*

Table 1. Comparison of Lung Histology in Bubble Oxygenator and Membrane Oxygenator Groups Before Lung Reperfusion[a]

	BO (n = 8)				MO (n = 8)				
Variable	−	+	+ +	+ + +	−	+	+ +	+ + +	*p* Value
Capillaries									
Endothelium	1	5	2	0	2	5	1	0	0.699
Erythrocytes	0	3	3	2	0	4	3	1	0.719
Leukocytes	1	5	2	0	2	5	1	0	0.699
Platelets	0	4	4	0	5	2	1	0	0.387
Alveoli									
Erythrocytes	0	6	1	1	2	5	0	1	0.389
Leukocytes	0	5	2	1	2	4	1	1	0.430
Plasma	2	4	1	1	5	2	1	0	0.204
Type I cells	3	4	1	0	4	3	1	0	0.852
Type II cells	0	2	3	3	0	1	4	3	1.000

[a] Pathological changes: normal (−), mild (+), moderate (+ +), and severe (+ + +).

BO = bubble oxygenator; MO = membrane oxygenator.

of lung type I cells ($p < 0.05$) (Table 2). These changes were less expressed in the MO group than in the BO group after lung reperfusion; in particular, there was less leukocyte and platelet accumulation in the lung microvasculature (Table 3).

Correlation

There was a significant correlation between the leukocyte and platelet sequestration in the lungs (RA–LA gradient) measured 15 minutes after lung reperfusion and the leukocyte and platelet accumulation in the lung microvasculature in histological findings from the individual data (Spearman's correlation coefficient: $r_s = 0.782$, $p < 0.05$ for leukocyte sequestration; $r_s = 0.786$, $p < 0.05$ for platelet sequestration).

Lung Water Content

A significantly reduced lung water content was found 30 minutes after CPB in the MO group as compared with that in the BO group (83.2% ± 2.4% versus 86.9% ± 1.4%; $p < 0.01$).

Comment

The increased leukocyte and platelet sequestration in the lung together with oxygen free radical release (expressed by plasma MDA concentration) and lung histological changes clearly indicate that lung injury during CPB is seen particularly after lung reperfusion with the use of a BO. In the BO group but not in the MO group, leukocyte and platelet RA–LA gradients occurred simultaneously with an increase in MDA concentration in plasma after reperfusion of the lungs. Clinically, the correlation of leukocyte sequestration and oxygen free radical release as expressed by MDA concentration after lung reperfusion was also observed in patients undergoing CPB with a BO [4]. This could support the general consensus that leukocyte sequestration and the consequent release of oxygen

Table 2. Comparison of Lung Histology Before and After Lung Reperfusion in Bubble Oxygenator Group[a]

	Before (n = 8)				After (n = 8)				
Variable	−	+	+ +	+ + +	−	+	+ +	+ + +	*p* Value
Capillaries									
Endothelium	1	5	2	0	0	1	5	2	0.021
Erythrocytes	0	3	3	2	0	1	4	3	0.509
Leukocytes	1	5	2	0	0	0	5	3	0.003
Platelets	0	4	4	0	0	1	3	4	0.046
Alveoli									
Erythrocytes	0	6	1	1	0	1	3	4	0.030
Leukocytes	0	5	2	1	0	2	2	4	0.151
Plasma	2	4	1	1	0	2	3	3	0.073
Type I cells	3	4	1	0	0	2	3	3	0.011
Type II cells	0	2	3	3	0	1	5	2	1.000

[a] Pathological changes: normal (−), mild (+), moderate (+ +), and severe (+ + +).

Table 3. Comparison of Lung Histological Changes Between Bubble Oxygenator and Membrane Oxygenator Groups After Lung Reperfusion[a]

	BO (n = 8)				MO (n = 8)				
Variable	−	+	++	+++	−	+	++	+++	*p* Value
Capillaries									
Endothelium	0	1	5	2	0	2	4	2	0.977
Erythrocytes	0	1	4	3	0	5	2	1	0.082
Leukocytes	0	0	5	3	0	5	2	1	0.018
Platelets	0	1	3	4	0	6	1	1	0.029
Alveoli									
Erythrocytes	0	1	3	4	0	2	3	3	0.719
Leukocytes	0	2	2	4	1	3	3	1	0.193
Plasma	0	2	3	3	0	6	0	2	0.141
Type I cells	0	2	3	3	1	4	1	2	0.250
Type II cells	0	1	5	2	0	0	5	3	1.000

[a] Pathological changes: normal (−), mild (+), moderate (++), and severe (+++).

BO = bubble oxygenator; MO = membrane oxygenator.

free radicals in the lung is one of the major causes leading to lung injury during CPB [15–18]. Apart from oxygen radicals, leukocytes have the potential to release other lysosomal enzyme products such as elastase as well as arachidonic acid metabolites upon activation [6, 7]. In a recent clinical study, Jansen and co-workers [19] showed that on reperfusion of the lungs, a leukocyte inflammatory reaction occurred with the release of tumor necrosis factor, correlating with postoperative vasodilation and blood pooling. This finding gives further indication that leukocyte activation during CPB, especially after lung reperfusion, plays an important role in initiating the whole-body inflammatory reaction after CPB.

Concomitant with the leukocyte sequestration in the lungs, a significant platelet sequestration after lung reperfusion was also found in this canine study. As known already, the vasoactive substances released from platelets such as serotonin and thromboxane A_2 might result in pulmonary vasoconstriction leading to lung injury [8–10]. Furthermore, platelet-derived growth factor, a release product from platelet granules upon activation, acts as a leukocyte inflammatory cofactor related to tissue injury [20]. However, in humans, the phenomenon of transpulmonary platelet sequestration was rarely seen, presumably because there are differences between dogs and humans regarding receptors on the platelet membrane.

The increased lung sequestration of leukocytes and platelets resulted in a significant increase of extravascular lung water in the BO group. This suggested that lung reperfusion injury during CPB is caused by a capillary leak syndrome including the damage of both endothelial and alveolar cells. The same sequence of events is observed in the early stage of adult respiratory distress syndrome [16, 17]. On the other hand, lung type II cell damage was found similarly in both MO and BO groups even before lung reperfusion in our study. This was most likely due to the mechanical ventilation of the animals because the main granule from type II cells, lung surfactant, is released during the period of mechanical ventilation [21]. Nevertheless, the combined lung injury from both lung endothelial cells and alveolar cells and consequently the increased extravascular lung water might cause lung malfunction after CPB, in particular, after the use of a BO but not an MO.

The differences between the BO and the MO groups regarding pulmonary leukocyte sequestration and lung reperfusion injury could not be simply explained by complement activation initiated by oxygenators because the differences in complement activation between the BO and the MO remain controversial [3, 18, 22]. In general, binding of C5a to the specific receptors on polymorphonuclear leukocytes promotes leukocyte aggregation. As a result, complement activation with release of anaphylatoxins C3a and C5a has been considered one of the causes of leukocyte activation during CPB [1–3]. However, other damaging effects such as the direct blood-gas interface as well as mechanical trauma in bubble oxygenation rather than in membrane oxygenation could also activate leukocytes by producing more cellular release products or activated plasma factors independent from complement activation. Therefore, these activated leukocytes will likely express more of their membrane-adherant receptors and then be more potent to adhere to pulmonary capillaries after lung reperfusion.

We conclude from our study that in a standardized canine CPB model, lung injury was started by lung reperfusion during CPB. However, the injury was correlated to the amount of leukocyte and platelet sequestration induced by the different types of oxygenators. In this regard, membrane oxygenation prevents pulmonary leukocyte and platelet accumulation as well as MDA generation, finally resulting in less lung injury than bubble oxygenation after lung reperfusion.

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References

1. Chenoweth DE, Cooper SW, Hugli TE, Stewart RW, Blackstone EH, Kirklin JW. Complement activation during cardiopulmonary bypass. Evidence for generation of C3a and C5a anaphylatoxins. N Engl J Med 1981;304:497–503.
2. Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–57.
3. Van Oeveren W, Kazatchkine MD, Descamps-Latscha B, et al. Deleterious effects of cardiopulmonary bypass. A prospective study of bubble versus membrane oxygenation. J Thorac Cardiovasc Surg 1985;89:888–99.
4. Royston D, Fleming JS, Desai JB, Westaby S, Taylor KM. Increased production of peroxidation products associated with cardiac operations. Evidence for free radical generation. J Thorac Cardiovasc Surg 1986;91:759–66.
5. Fleming JS, Royston D, Westaby S, Desai JB, Taylor KM. Neutrophil malondialdehyde content as an indicator of activation during cardiopulmonary bypass. Life Support Syst 1986;4:257–61.
6. Riegel W, Spillner G, Schlosser V, Hörl WH. Plasma levels of main granulocyte components during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1988;95:1014–9.
7. Faymonville ME, Deby-Dupont G, Larbuisson R, et al. Prostaglandin E_2, prostacyclin, and thromboxane changes during nonpulsatile cardiopulmonary bypass in humans. J Thorac Cardiovasc Surg 1986;91:858–66.
8. Westaby S. Organ dysfunction after cardiopulmonary bypass. A systemic inflammatory reaction initiated by the extracorporeal circuit. Intensive Care Med 1987;13:89–95.
9. Greeley WJ, Bushman GA, Kong DL, Oldham HN, Peterson MB. Effects of cardiopulmonary bypass on eicosanoid metabolism during pediatric cardiovascular surgery. J Thorac Cardiovasc Surg 1988;95:842–9.
10. Martin BA, Dahlby R, Nicholls I, et al. Platelet sequestration in lung with hemorrhagic shock and reinfusion in dogs. J Appl Physiol 1981;50:1306–12.
11. Edmunds LH Jr, Ellison N, Colman RW, et al. Platelet function during cardiac operation. Comparison of membrane and bubble oxygenators. J Thorac Cardiovasc Surg 1982;83:805–12.
12. Van den Dungen JJAM, Karliczek GF, Brenken U, Homan van der Heide JN, Wildevuur CRH. Clinical study of blood trauma during perfusion with membrane and bubble oxygenation. J Thorac Cardiovasc Surg 1982;83:108–16.
13. Van Oeveren W, Dankert J, Wildevuur CRH. Bubble oxygenation and cardiotomy suction impair the host defense during cardiopulmonary bypass. A study in dogs. Ann Thorac Surg 1987;44:523–8.
14. Su BH, Shi BZ. Calculation of exact probability of contingency tables. Chin J Health Stat 1987;4:16–9.
15. Tate RM, Repine JE. Neutrophils and the adult respiratory distress syndrome. Am Rev Respir Dis 1983;128:552–9.
16. Rinaldo JE, Rodgers R. Adult respiratory distress syndrome: changing concepts of lung injury and repair. N Engl J Med 1982;396:900–9.
17. Maggart M, Stewart S. The mechanisms and management of noncardiogenic pulmonary edema following cardiopulmonary bypass. Ann Thorac Surg 1987;43:231–6.
18. Hammerschmidt DE, Stroncek DF, Bowers TK, et al. Complement activation and neutropenia occurring during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1981;81:370–7.
19. Jansen NJG, Van Oeveren W, Vander Broek L, et al. Inhibition of the reperfusion phenomena in cardiopulmonary bypass by dexamethasone. J Thorac Cardiovasc Surg (in press).
20. Lanser ME, Brown GE, Garcia-Aguilar J. Neutrophil CR3 induction by platelet supernatants is due to platelet-derived growth factor. Surgery 1988;104:287–91.
21. Nicholas TE, Barr HA. The release of surfactant in a rat lung by brief periods of hyperventilation. Respir Physiol 1983;52:69–83.
22. Cavarocchi NC, Pluth JR, Schaff HV, et al. Complement activation during cardiopulmonary bypass. Comparison of bubble and membrane oxygenators. J Thorac Cardiovasc Surg 1986;91:252–8.

Cardiopulmonary Perfusion and Cerebral Blood Flow in Bilateral Carotid Artery Disease

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The fear of cerebral complications after cardiopulmonary bypass in patients with heart disease and severe carotid artery disease has led many authors to suggest combined approaches in these patients. The pathogenetic mechanism for stroke is based partly on the stenotic narrowing of the carotid artery. A diameter reduction of 75% is frequently considered hemodynamically significant and indicative of an increased risk for neurological morbidity. We studied the cerebral blood flow in 7 patients undergoing coronary artery bypass grafting who also had severe bilateral carotid disease. The results were compared with the results in 17 patients without carotid disease who had bypass grafting. The cerebral blood flow was measured by xenon 133 washout technique before, during, and after cardiopulmonary bypass with moderate hypothermia. Acid-base regulation was according to the alpha-stat theory, and blood pressure was kept greater than 50 mm Hg. The cerebral blood flow levels ($mL \cdot 100\ g^{-1} \cdot min^{-1}$) before, during, and after cardiopulmonary bypass in the study group (30 ± 11, 31 ± 8, 47 ± 20) (mean ± standard deviation) were almost identical to those in the control group (30 ± 11, 28 ± 8, 47 ± 12). The cerebral blood flow levels for the left and right hemispheres in the group with carotid disease were comparable and within normal ranges. In 2 patients, slight differences were noted between hemispheres, and this finding may indicate an increased risk for ischemia. These patients, however, did not show any signs of postoperative deficit. The flow limitations of critical carotid stenoses do not seem to imply a risk for cerebral hypoperfusion if cardiopulmonary perfusion is performed in a controlled manner. The indications for combined procedures in patients with concomitant disease should be based on criteria other than the influence of flow-limiting stenoses.

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Patients with concomitant carotid and coronary arteriosclerotic disease present a special problem for the cardiac surgeon. Should the carotid disease in any way affect the strategy of cardiopulmonary bypass (CPB), or should a combined or staged operation on both the carotid and coronary arteries be undertaken? The issue was recently reviewed by Newman and Hicks [1], who concluded that a consensus on the most appropriate management of coexisting disease is still lacking.

For editorial comment, see page 532.

The rationale for combined or staged procedures, where the carotid disease is treated before CPB, is based on the assumption that cerebral blood flow (CBF) will be insufficient during all or part of the cardiac procedure, that emboli from the carotid stenoses may be detached during perfusion, or that both of these situations will occur. The severity of stenosis in the internal carotid artery is, of course, important to consider. In the literature [1–3], a 75% to 80% stenosis is frequently regarded as major, at least in combination with an insufficiency of the circle of Willis. Reversed blood flow in the ophthalmic arteries indicates a critical stenosis [4].

The capacity to compensate for alterations in blood pressure, or blood oxygen content by autoregulation of CBF, plays an important part in our response system for maintenance of normal brain function. The autoregulation is normally preserved during CPB, at least when acid-base regulation according to the alpha-stat theory has been applied [5–9]. The blood pressure limitations of autoregulation in the normal awake human range between about 50 and 150 mm Hg. During CPB, the range is not established, but the lower limit for autoregulation may not always apply.

In this study, we compare CBF before, during, and after CPB in patients who have advanced bilateral stenotic or occlusive carotid disease with CBF in patients without stenoses in the carotid arteries.

Material and Methods

Seven patients referred to our department for coronary artery bypass grafting (CABG) with concomitant bilateral carotid artery disease were monitored with CBF measurements. These data were later compared with those from 17 patients without carotid involvement who also underwent CABG. The severity of stenosis was assessed with ultrasound or Doppler techniques as part of the preoper-

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Table 1. Summary of Data on Group With Carotid Artery Disease

Patient No.	Carotid Lesion		Flow Direction in Ophthalmic Artery		Symptom	Preop Treatment
	Left	Right	Left	Right		
1	Stenotic	Stenotic	?	+	TIA, temporary loss of speech	Dicumarol
2	Occluded	Stenotic	?	+	TIA, sensory deprivation in right arm and face	None
3	Stenotic	Stenotic	−	−	TIA, amaurosis fugax	None
4	Occluded	Stenotic	−	+	None	None
5	Stenotic	Stenotic	−	−	None	None
6	Occluded	Occluded	−	−	None	None
7	Occluded	Stenotic	−	+	TIA, numbness in left leg or both legs	None

TIA = transient ischemic attack; + = normal direction; − = reversed flow; ? = indecisive.

ative investigation. The hemodynamic significance of the lesion was evaluated by the examining neurologist. A reversed or indecisive flow in the ophthalmic artery in combination with the finding of increased or absent flow-velocity signal in the carotid artery indicated a stenosis or occlusion of major degree. The patients were interviewed concerning preoperative neurological deficits. Detailed information on the carotid disease is given in Table 1.

The 17 patients without carotid artery disease served as healthy controls. Previously, measurements of CBF in these patients were used to study carbon dioxide response [10] and autoregulation [5]. Group characteristics are shown in Table 2.

Anesthesia and Surgical Techniques

All patients were premedicated with fentanyl (0.025 to 0.05 mg) and droperidol (1.25 to 2.5 mg). Induction and maintenance of anesthesia was performed as described previously [5] but consisted mainly of a regimen of droperidol and high-dose fentanyl combined with inhalation of a 50% mixture of nitrous oxide in oxygen before and after CPB. During CPB, no volatile anesthetics were used. Systolic blood pressure in the study group was kept greater than 70 mm Hg, which in some patients necessitated the help of dopamine hydrochloride or norepinephrine infusions. A depolarizing muscle relaxant was used at the induction of anesthesia (succinylcholine chloride) and at the onset of bypass (alcuronium chloride), but rarely otherwise. Distal coronary anastomoses were made with the aorta cross-clamped during cardioplegic hypothermic arrest, followed by the proximal anastomoses with a side-biting clamp on the beating heart.

Table 2. Demographic Data on the Two Groups[a]

Variable	Study Group (n = 7)	Control Group (n = 17)	*p* Value
Age (y)	67 ± 5	54 ± 8	0.05
No. of grafts	4 ± 1.4	3.9 ± 0.9	NS
Total perfusion time (min)	104 ± 33	111 ± 26	NS
Perfusion time at measurement 2 (min)	37 ± 22	40 ± 26	NS
Time after CPB for measurement 3 (min)	11 ± 5	18 ± 14	NS
Cross-clamp time (min)	52 ± 15	61 ± 14	NS

[a] Data are shown as the mean ± the standard deviation.

CPB = cardiopulmonary bypass; NS = not significant.

Cardiopulmonary Bypass

STUDY PATIENTS. Cardiopulmonary bypass was performed using a Stöchert heart-lung machine with a roller pump in the nonpulsatile mode or, if blood pressure was low (lower than 50 mm Hg), in the pulsatile mode for shorter periods until pharmacological restitution had been made. Six patients were perfused using a bubble oxygenator (Bentley BOS 10, 5 patients; Cobe Optiflow II, 1 patient). In 1 patient, a membrane oxygenator (Cobe CML) was used. An arterial filter (pore size, 40 μm) was used in all patients. The bypass circuit consisted of polyvinyl chloride with silicon in the pump head. The circuit was primed with 2,000 mL of Ringer's lactate solution, 250 mL of 15% mannitol, and 75 mmol/L of Addex tromethamine. Onset of bypass was slow to avoid a rapid decrease in blood pressure. The patients were perfused at moderate hypothermia (around 30°C rectal temperature) and rewarmed to 34°C before weaning from bypass.

CONTROL PATIENTS. Pumping, bypass circuit, priming, and temperature regimens were similar to those in the study patients. Patients were oxygenated using membrane oxygenators (Cobe CML, 9 patients) or bubble oxygenators (Cobe Optiflow II, 8 patients). Control of blood pressure in this group was not as strict, but the mean arterial blood pressure was rarely less than 50 mm Hg. To enhance rewarming, a few patients received a small dose of chlorpromazine hydrochloride (5 to 10 mg). Drugs affecting brain metabolism or blood flow, apart from the anesthetic agents, were otherwise avoided.

Acid-Base Strategy

Alpha-stat regulation is routinely applied at our institution. All blood gases were analyzed at 37°C, and no correction for deviations in body temperature was performed.

Cerebral Blood Flow Measurements

Cerebral blood flow was measured using the xenon 133 method described previously [5, 10]. In the group with carotid disease, all measurements were made by injection of xenon 133 into the ascending aorta (0.1 to 0.3 GBq) except in 2 patients (patients 2 and 7) in whom xenon 133 (0.5 GBq) was administered intravenously for the measurements before and after CPB. In 9 control patients, intraarterial injection of the tracer substance (0.1 to 0.2 GBq) was performed through a catheter inserted during operation and positioned in the brachiocephalic trunk or internal carotid artery. In the remaining 8 control patients, this technique was applied only during CPB, and the measurements obtained before and after CPB were conducted with the intravenous method.

Clearance of the tracer was monitored from the expired air (intravenous measurements) and from the right hemisphere (control patients) using four scintillation detectors covering the parietotemporal region. In the study patients, a single detector was placed over each hemisphere. Background or residual activity was recorded before each measurement.

The Novo cerebrograph model 10a was used for collection and subsequent calculation of data by the method of Olesen and co-workers [11] (intraarterial measurements) and Risberg and associates [12] (intravenous measurements). All hemispheric CBF values were either mean values from four small detectors or values from a single large detector and correspond mainly to the gray matter flow. They were corrected for changing xenon solubility in blood caused by variations in the hemoglobin concentration [13].

The influence of the partial pressure of arterial CO_2 on the CBF values was compensated for by recalculation of CBF values corresponding to a partial pressure of arterial CO_2 of 5.3 kPa (40 mm Hg) using the CO_2 reactivity 9.1 mL/kPa CO_2 change (1.2 mL/mm Hg) reported previously [10].

Cerebral blood flow was measured from both hemispheres in the 7 study patients before, during, and after CPB. At each measurement, arterial blood was sampled for analysis of hemoglobin concentration, partial pressure of arterial CO_2, partial pressure of arterial oxygen, and pH. Arterial blood pressure and central venous pressure were recorded. The temperature was measured in the esophagus or external auditory meatus. Originally, in the control patients, two CBF measurements were performed before, during, and after CPB to evaluate either CO_2 reactivity [10] or autoregulation [5]. The measurements chosen in the control group to match the measurements in the study group were those that had an equal time relation to intraoperative events, as is evident from Table 2.

Statistical Analysis

Mean values are given ± one standard deviation. The significance level was 0.05 if not otherwise indicated. For comparison between groups, an unpaired *t* test was used. For evaluation of changes within groups, one-way analysis of variance was performed. All calculations were made on RS/1 (BBN Software Corp, Cambridge, MA).

Results

Although the CBF level in the patients with carotid artery disease (raw data from Table 3, including both hemispheres) was significantly affected by the measurement conditions (before, during, after CPB) ($p = 0.05$, analysis of variance) there was no difference between these patients and the control group (Table 4) with reference to the right hemisphere (the only hemisphere measured in the control group).

The mean arterial blood pressure before CPB tended to be slightly greater in the study group. Hemodilution led to a significant decrease in hemoglobin levels at the onset of CPB. This was more pronounced in the group with carotid artery disease. Both groups showed greater CBF levels after CPB than before CPB. During CPB, the CBF increase was inhibited by the decrease in temperature.

The immediate postoperative outcome was excellent for all patients in the study group but 1. Patient 3, who also had impairment of the vertebral circulation, had respiratory and nutritional difficulties postoperatively. On the 11th postoperative day, he became septic, had to be reintubated, and thereafter could not be weaned from the ventilator. There were no signs of focal neurological impairment. He was transferred to the local hospital and died a month later of multiorgan failure. Patient 1 continued to have intermittent speech difficulties and underwent a right-sided carotid endarterectomy 14 months after CABG. He is now well. The neurological status of the remaining patients in the study group is as it was preoperatively. One patient in the control group had a right-sided hemiparesis, which was evident at clinical examination 24 hours postoperatively. A computed tomographic scan revealed a left-sided infarction.

Comment

The optimal surgical approach to patients with concomitant coronary and carotid artery disease is still a matter of controversy. Rationales for both combined (during the same anesthesia) and staged procedures can be found in the literature. A recent review by Newman and Hicks [1] concluded that patients with carotid artery stenoses of more than 75% have a major risk for stroke as do patients with ulcerated plaques or bilateral disease.

Table 3. Individual Mean Values of Cerebral Blood Flow in Left and Right Hemispheres in Study Group[a]

	Left			Right		
Patient No.	Before CPB	During CPB	After CPB	Before CPB	During CPB	After CPB
1	16	28	22	15	34	25
2	31	29	84	34	21	66
3	30	27	33	31	30	35
4	24	30	29	21	26	35
5	30	33	33	31	30	32
6	27	45	56	31	48	57
7	35	32	59	49	31	79
Mean ± SD	28 ± 6	32 ± 6	45 ± 22	30 ± 11	31 ± 8	47 ± 20

[a] The cerebral blood flow values were corrected to a partial pressure of carbon dioxide = 5.3 kPa (40 mm Hg).

CPB = cardiopulmonary bypass; SD = standard deviation.

Ivey and co-workers [14] recommended that patients with coronary heart disease and asymptomatic carotid artery stenosis exceeding 80% undergo CABG followed by carotid endarterectomy in a staged procedure. If symptomatic with reference to the carotid disease, carotid endarterectomy should be done first and CABG later. A combined procedure should be undertaken only for patients with severe symptomatic disease in combination with unstable angina, triple-vessel disease with impaired left ventricular function, or left main disease. These guidelines were basically supported by Graor and Hetzer [15], who also included patients with bilateral disease among those in need of a combined operation.

The literature contains numerous reports on the safety and feasibility of combined operations on coronary and carotid arteries. Few reports deal with the asymptomatic patient and the results of CABG alone. There seems to be an increased risk for stroke in patients with carotid bruits after heart operation, the risk, however, being of the same magnitude as for patients with postoperative atrial fibrillation, mitral regurgitation, a history of myocardial infarction, or congestive heart failure [16]. The indication for carotid endarterectomy in asymptomatic disease is questionable [17, 18], and prospective, randomized trials are still warranted. Hertzer and co-workers [19] found the stroke rate to be as high as 7.8% in patients with asymptomatic unilateral disease who underwent either staged or combined procedures. The stroke rate was higher for staged than for combined procedures.

The occurrence of perioperative stroke in CABG patients was not related to bilateral or contralateral occlusive disease in a study by Perler and colleagues [20]. The postoperative mortality was higher in older patients, and an increased risk was found in patients with bilateral

Table 4. Cerebral Blood Flow in Right Hemisphere and Related Variables for the Two Groups Before, During, and After Cardiopulmonary Bypass[a]

Variable	Group	Before	During	After	ANOVA
CBF_{40}	Study	30 ± 11	31 ± 8	47 ± 20	NS
($mL \cdot 100\ g^{-1} \cdot min^{-1}$)	Control	30 ± 11	28 ± 8	47 ± 12	0.05
$PaCO_2$ (kPa)	Study	5.1 ± 0.5	4.9 ± 0.5	4.8 ± 0.6	NS
	Control	4.7 ± 0.4	4.9 ± 0.8	5.1 ± 0.9	NS
Arterial blood pressure	Study	86 ± 11	74 ± 16	78 ± 9	NS
(mm Hg)	Control	71 ± 13	65 ± 20	71 ± 20	NS
pH (U)	Study	7.40 ± 0.04	7.41 ± 0.06	7.40 ± 0.06	NS
	Control	7.43 ± 0.06	7.41 ± 0.08	7.39 ± 0.07	NS
Hemoglobin (g/L)	Study	131 ± 18	84 ± 17	92 ± 15	0.05
	Control	140 ± 12	99 ± 12	109 ± 14	0.05
Temperature (°C)	Study	35.3 ± 0.7	29.1 ± 2.4	35.8 ± 0.7	0.05
	Control	34.8 ± 0.5	29.3 ± 1.3	36.1 ± 1.1	0.05

[a] Data are shown as the mean ± the standard deviation.

ANOVA = analysis of variance; CBF_{40} = cerebral blood flow corrected to $PaCO_2$ of 5.3 kPa (40 mm Hg) (see text for further details); NS = not significant; $PaCO_2$ = partial pressure of arterial carbon dioxide at 37°C (no temperature correction performed).

carotid disease or contralateral occlusion. Schultz and associates [21] found no differences in operative mortality or late survival between a group of 50 asymptomatic patients with hemodynamically significant carotid stenosis and a matched control group, both groups having CABG. There was a greater risk for late neurological deficits in the group with carotid stenosis, but the medical treatment of these patients was not discussed.

What are the hazards of cardiopulmonary perfusion in patients with carotid disease? There are two primary hazards: (1) embolic stroke after embolization from atherosclerotic plaques during CPB and (2) decreased CBF because of severe stenotic or occlusive lesions combined with a defect in the circle of Willis. The latter is especially important in combination with low perfusion pressure or venous drainage problems and associated elevation in the central venous pressure.

Powers and colleagues [4] used positron emission tomography to study the hemodynamic influence of a unilateral carotid stenosis on CBF and metabolism. They found a poor correlation between the degree of stenosis and intracerebral hemodynamics, thus illustrating the compensatory capacity of the internal and external collaterals. Their results further indicated that ". . . little rationale exists for using the degree of carotid stenosis to decide whether a patient may be at increased risk for stroke on hemodynamic grounds or whether cerebral symptoms are caused by poor perfusion."

The autoregulatory capacity of the brain normally makes it possible for us to tolerate a wide range of blood pressure changes without major alterations in CBF. However, when the capacity for autoregulation is exhausted, the risk for brain ischemia can be immediate should the flow decrease.

Autoregulation during hypothermic CPB in otherwise healthy individuals seems to be intact provided acid-base regulation is maintained according to alpha-stat management and blood pressure ranges are within safe limits for the autoregulatory curve [5, 6, 7, 9]. It can be speculated that the lower limit for autoregulation during hypothermic CPB is decreased as a result of both lower blood viscosity by hemodilution and lower metabolism at lower temperatures. This, however, remains to be proven.

Testing autoregulation using pairwise measurements was not performed in the group with carotid disease. The CBF pattern, however, performed in the same manner as in patients without carotid disease in whom autoregulation and CO_2 reactivity had been studied and found normal. The flow levels of the hemispheres were comparable and in agreement with the results of other investigators [6, 7, 9].

The flow values in 5 of the study patients indicated an even distribution to the hemispheres. In patient 2, flow to the occluded side was higher than to the stenotic side during and after CPB. In patient 7, CBF during CPB was similar in both hemispheres but was lower before and after CPB in the occluded side. In both patients, xenon was administered intravenously before and after CPB. The intravenous CBF method gives a somewhat increased error level for the CBF measurements but can hardly explain the interhemispheric differences. The hemispheric CBF for both patients was in the normal range during CPB, but this does not exclude the possibility of regional ischemia resulting in a postperfusion hyperemia. If this were the case, it would also indicate an increased risk for ischemic lesions during CPB in these 2 patients. However, they did not show any postoperative deficits.

This study confirms the results of Powers and coauthors [4]. It shows that despite severe bilateral stenoses or occlusions of the carotid arteries, even in combination with vertebral disease, the mean hemispheric CBF values can be kept at levels at which the risk for ischemic brain damage must be considered small, though not entirely negligible. Perfusion pressure should be kept in a range where autoregulation is retained, and a normal acid-base balance should be maintained according to the alpha-stat method.

The underlying cause of perioperative stroke during open heart operations is multifactorial and can be related to both the CPB procedure and the surgical handling of the heart and aorta. In patients with concomitant cardiac and carotid disease, there is an additional risk for stroke depending on the degree of carotid involvement. This risk appears to be related more to the surface pathology of the carotid lesion than to the degree of stenosis per se.

In conclusion, this study shows that CPB in patients with hemodynamically significant bilateral carotid disease can be achieved without impairment of mean hemispheric CBF as long as the perfusion strategy is in accordance with preserved autoregulation and CO_2 reactivity. The necessity for combined surgical procedures in asymptomatic patients is questionable, and the indication for combined procedures should be based on criteria other than the flow-limiting influence of carotid disease.

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References

1. Newman DC, Hicks RG. Combined carotid and coronary artery surgery: a review of the literature. Ann Thorac Surg 1988;45:574–81.
2. Chambers BR, Norris JW. The case against surgery for asymptomatic carotid stenosis. Stroke 1984;15:964–7.
3. Roederer GO, Langlois YE, Jager KA, et al. The natural history of carotid arterial disease in asymptomatic patients with cervical bruits. Stroke 1984;15:605–13.
4. Powers WJ, Press GA, Grubb RL, Gado M, Raichle ME. The effect of hemodynamically significant carotid artery disease on the hemodynamic status of the cerebral circulation. Ann Intern Med 1987;106:27–35.
5. Johnsson P, Messeter K, Ryding E, Nordström L, Ståhl E. Cerebral blood flow and autoregulation during hypothermic cardiopulmonary bypass. Ann Thorac Surg 1987;43:386–90.
6. Govier AV, Reves JG, McKay RD, et al. Factors and their influence on regional cerebral blood flow during nonpulsatile cardiopulmonary bypass. Ann Thorac Surg 1984;38:592–600.
7. Murkin JM, Farrar JK, Tweed WA, McKenzie FN, Guiraudon GM. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. Anesth Analg 1987;66:825–32.

8. Murkin JM. Cerebral hypoperfusion during cardiopulmonary bypass: the influence of $PaCO_2$. In: Hilberman M, ed. Brain injury and protection during heart surgery. Boston: Martinus Nijhoff, 1988:47–66.
9. Venn GE. Cerebral vascular autoregulation during cardiopulmonary bypass. Perfusion 1989;4:105–13.
10. Johnsson P, Messeter K, Ryding E, Kugelberg J, Ståhl E. Cerebral vasoreactivity to carbon dioxide during cardiopulmonary perfusion at normothermia and hypothermia. Ann Thorac Surg 1989;48:769–75.
11. Olesen J, Paulsen OB, Lassen NA. Regional cerebral blood flow in man determined by the initial slope of the clearance of intra-arterially injected ^{133}Xe. Stroke 1971;2:519–40.
12. Risberg J, Ali Z, Wilson EM, Wills EL, Halsey JH Jr. Regional cerebral blood flow by 133 xenon inhalation. Stroke 1975;6: 142–8.
13. Veal N, Mallet BL. The partition of trace amounts of xenon between human blood and brain tissues at 37°C. Phys Med Biol 1965;10:375–80.
14. Ivey TD, Strandness ED, Williams DB, et al. Management of patients with carotid bruit undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg 1984;87:182–9.
15. Graor RA, Hertzer NR. Management of coexistent carotid artery and coronary artery disease. Stroke 1988;19:1441–4.
16. Reed GL III, Singer DE, Picard EH, DeSanctis RW. Stroke following coronary artery bypass surgery. A case-control estimate of the risk from carotid bruits. N Engl J Med 1988;319:1246–50.
17. Schlosser V, von Reutern GM, Binbaum D, et al. Zur Operationsindikationen bei asymptomatischer Arteria-carotis-interna-Stenose allein und in Zusammenhang mit herzchirugischen Eingriffen. Herz 1988;13:263–9.
18. Dyken ML. Carotid endarterectomy studies: a glimmering of science [Editorial]. Stroke 1986;17:355–8.
19. Hertzer NR, Loop FD, Beven EG, O'Hara PJ, Krajewski LP. Surgical staging for simultaneous coronary and carotid disease: a study including prospective randomization. J Vasc Surg 1989;9:455–63.
20. Perler BA, Burdick JF, Minken SL, Williams GM. Should we perform carotid endarterectomy synchronously with cardiac surgical procedures? J Vasc Surg 1988;8:402–9.
21. Schultz RD, Sterpetti AV, Feldhaus RJ. Early and late results in patients with carotid disease undergoing myocardial revascularization. Ann Thorac Surg 1988;45:603–9.

animals with rejection showed evidence of pneumonia on histological examination of the open-lung biopsy specimen. None of the cultures from the rejecting lung tissue grew bacteria.

Comment

To date, clinicians in active lung-transplantation programs rely on clinical information for an imprecise diagnosis of lung rejection. Typically, the patient experiences a low-grade temperature elevation, leukocytosis, an increased alveolar-arterial oxygen gradient, a subjective feeling of lethargy and dyspnea, and a radiological perihilar flare or infiltrate. This constellation of symptoms and signs could not differentiate rejection from pneumonia, atelectasis, or pulmonary edema. Transbronchial biopsy as advocated by the Papworth Hospital group [12, 13] is now considered to be the gold standard for determining the presence of rejection. Using both transbronchial biopsy and BAL, which will show the presence of pathogens in the distal airway, it is often possible to determine the likelihood of whether rejection, infection, or a combination of these is present. The specificity or sensitivity of these two techniques remains to be evaluated. Not infrequently, particularly when results of transbronchial biopsies and BAL are not conclusive, treatment strategies are formulated, and the diagnosis is made depending on the response to therapy.

The lack of a reliable method to determine the cause of lung allograft dysfunction signifies the need to identify new investigational techniques that are safe, accurate, and reproducible. In our animal model, specimens obtained by transbronchial biopsy were frequently scarce or were not representative of changes within the lung. We attributed this to the heterogeneity of lung changes in rejection or infection and the fact that lung injury can frequently be missed depending on the site of the transbronchial or percutaneous needle biopsy. It is perhaps for this reason that the need arises for numerous (more than eight) biopsies to achieve good yield, as in the Papworth Hospital experience [13].

Soon after transplantation, allografts accumulate various cellular and humoral factors, the function of which is to both reject and accommodate the new tissue. Recent studies have centered on several questions: What cells accumulate at the site of the allograft? Which ones are essential for graft destruction? What factors recruit them to the rejection site? An advantage of working with BAL cells in lung allograft rejection is that no special preparation such as enzymatic treatment of heart and kidney tissue is required to separate the lymphocytes before studying their surface marker or function, and hence no selection of specific lymphocyte subpopulation can occur [14, 15]. A variety of host cells have been shown to migrate to kidney and heart allografts, including T cells, immunoglobulin-bearing cells (B cells), natural killer cells, macrophages, and neutrophils. One can identify specific antidonor cytotoxic T-cell activity, nonspecific macrophage-mediated killing, and antibody-dependent cell-mediated cytotoxicity—all possible contributors to allograft destruction.

Finn and co-workers [16] examined the T-cell repertoire in allograft kidneys from both cadaver donors and living related donors. T lymphocytes obtained from needle biopsy specimens at the time of rejection were grown in vitro. Cell lines stimulated specifically by donor cells or nonspecifically by IL-2 showed both cytotoxic-suppressor (CD8+) and helper/inducer (CD4+) subpopulations. Functionally, however, the predominant cell type observed was a cytotoxic T-cell CD8+ when stimulation was specific for donor class I antigens and CD4+ when specific for donor class II antigens. All the cell lines consisted of activated T cells expressing receptors for IL2 and a high level of HLA-DR antigens in addition to Pan T-cell markers (T3, T11, and Leu 1). No cells bearing NK markers were detected. The predominance of cytotoxic T cells, which were highly toxic at very low effector to target cell ratios, implicates them as very likely effectors of tissue destruction in vivo [16].

In an attempt to determine the usefulness of PBL cell analysis in the monitoring of rejection after renal transplantation, Shenton and associates [17] examined PBL lymphocyte phenotypes 4 days after transplantation. The ratio of CD4+ to CD8+ cells was found to be lower in patients who showed two or more rejection episodes. The percentage of B cells, NK cells, and IL2 receptors on T cells was not found to be related to the rejection patterns in these kidney transplant recipients. In a similar manner, Lippolitis and colleagues [18] reported on the routine use of conventional and monoclonal antibody fluorescent staining of PBL cells to monitor heart transplant patients. They observed activation of PBL T cells when rejection occurred and was confirmed by endomyocardial biopsy. However, they alluded to the fact that T-cell activation was also noted in PBL T-cells of patients when episodes of viral or bacterial infections were encountered, thus indicating the nonspecificity of such T-cell activation. Furthermore, it has been shown by our group [19] and others [20] that PBL analysis may not reflect changes within the particular organ affected. Indeed, the idea of compartmentalization of immune response into specific target organs appears to be more accepted [20], hence the importance of pursuing the investigation of changes in the allograft itself and comparing those changes with changes in PBL samples.

The use of BAL as a method of analyzing lung cells for the purpose of detecting the type and severity of lung injury has recently gained increasing interest. It is now used to examine the mechanisms of lung injury in asthma, sarcoidosis, hypersensitivity pneumonitis, and infectious pneumonia [4]. The idea that BAL may be useful in detecting changes within the lung that may be specific for allograft rejection or infection is not new. As early as 1975, Achterrath and Veith [21] suggested that BAL analysis might provide an index for lung allograft rejection. They described the use of conventional stains such as periodic acid-Schiff and Giemsa techniques to attempt recognition of BAL cells. However, these conventional stains are now recognized to be not completely reliable in determining the type of cells in BAL samples. It is particularly difficult to differentiate between lymphocytes and macrophages. In addition, the separation of lymphocytes and macrophages into functional subsets has made the value of morphological differentiation unimportant.

Emeson and colleagues [22] used the nonspecific lectin-dependent cell-mediated cytotoxicity assay to quantitate cytotoxic and suppressor cells in BAL samples from nonrejecting and rejecting canine allotransplant lungs. Normal lungs and biopsy-proven nonrejecting lung allografts showed a low level of cytotoxicity, whereas rejecting lung allografts showed a wide range of cytotoxicity from lymphocytes harvested in BAL samples. Interesting were the observations that nonseparated BAL cells containing alveolar macrophages showed no cytotoxicity and that the addition of alveolar macrophages to separate lymphocytes abrogated T-cell cytotoxicity at all effector/target cell ratios. Emeson and colleagues concluded that an increased level of cytotoxicity must exist in BAL samples from rejecting lungs and that alveolar macrophages may play an important role in the suppression of cytotoxic T cells and hence attempt to prevent rejection. The major value of this work lies in the fact that changes in BAL cell cytotoxicity were noted at an early phase of lung rejection when the only pathological change was that of mononuclear cellular infiltration around small vessels, a change that is usually clinically concealed and precedes the latter phase of alveolar space involvement when radiological changes become manifest. The predictive value of the lectin-mediated cytotoxicity assay and a quantitative correlation between the degree of cytotoxicity and the extent of rejection were, however, not determined. The specificity and sensitivity of this test and its ability to differentiate rejection from other forms of lung injury are not yet known.

At the University of Pittsburgh, BAL has been used to study changes in heart-lung transplant recipients. Griffith and associates [23] observed an increased spontaneous proliferation of BAL cells early after lung transplantation as a result of infection between donor and recipient cells. Three to 5 months later, spontaneous proliferation of BAL cells appeared to be associated with *Pneumocystis carinii* infection. Such lymphocytes frequently respond to interleukin-2, a finding suggesting the presence of activated T cells. The same research group [24] also presented evidence that BAL lymphocytes exhibit donor-specific primed lymphocyte test reactivity during clinically diagnosed acute episodes of rejection (ie, rapidly progressive radiographic infiltrates that resolve with increased immunosuppression). Successful treatment with increased immunosuppression in some patients led to the disappearance of primed lymphocyte test reactivity of subsequent BAL samples. Gryzan and co-workers [25] have shown that the number of BAL cells recovered from heart-lung transplant recipients is greatly increased compared with normal values. During acute rejection, there is an increased number of macrophages, CD8-positive T cells, and neutrophils. During infection, particularly with *P carinii* and cytomegalovirus, both CD4 and CD8 cells are markedly increased [25]. This increase, however, was not significant. This may be attributed to the paucity of a pure form of rejection without some mild infection or, in the case of the reverse, the lack of occurrence of viral or protozoan infection without a mild form of rejection. Hence, attempts to identify a particular pattern of cellular changes specific to one type of lung injury or another may be impossible to achieve in the clinical lung transplantation setting. The use of experimental models of controlled infection or rejection becomes obvious.

In this study, we attempted to examine changes that occur in BAL cells in the presence of lung allograft rejection and compare them with the changes that occur in the presence of lung infection. Although the setting of clinical lung allograft rejection can involve many variables, including its occurrence in the presence of cyclosporine, azathioprine, and steroid therapy as well as its occurrence in the possible presence of opportunistic infections such as cytomegalovirus, we chose to start by examining the basic changes expected to occur in the presence of allograft rejection alone. Early immunosuppression was essential during the first few days to take the grafts over the initial period of implantation response, which frequently occurs within the first 5 days after transplantation in dogs [5]. We used monoclonal antibodies raised specifically against canine lymphocytes and monocytes to analyze changes that occur in rejecting lungs and to attempt to see if differences in cellular subset composition occur between the rejecting and infected lungs. We found that the percentage of DT2-labeled cells was significantly higher in BAL samples from rejecting lungs as compared with samples from infected lungs. In addition, the PBL/BAL ratio of DT2-labeled cell percentage was found to be significantly higher in the pneumonia group compared with the acute rejection group.

Urban and associates [26] reported that antibody DT2 directed at T cells inhibited MLC responses and cytotoxic lymphocyte activity only when lymphocytes were treated before culture (day 0), but they had no substantial effect on these functions when cells were treated after 6 days in culture. The mean percentage of DLY-1 cells in BAL fluid from rejecting lungs appeared to be lower than that in PBL samples from the same group, whereas the percentage of DLY-1 cells in BAL and PBL samples from the pneumonia group were similar. Antibody DLY-1, which reacts with canine lymphocytes and monocytes, was found to abrogate MLC responses and cytotoxic lymphocyte activity when responder cells were treated on day 0. When cells were treated after 6 days in culture, MLC responses were reduced to 47% of control, whereas cytotoxic lymphocyte activity increased slightly [6].

The E11 antibody was characterized by Ledigus (personal communication, 1990) to identify most of the alloantigen-stimulated suppressor cells. We found that the percentage of E11-labeled cells in PBL samples from the rejection group was significantly higher than that in the pneumonia group. Even though the percentage of E11-labeled cells in BAL samples from the rejection group also appeared to be higher than that in the pneumonia group, no significant difference was found.

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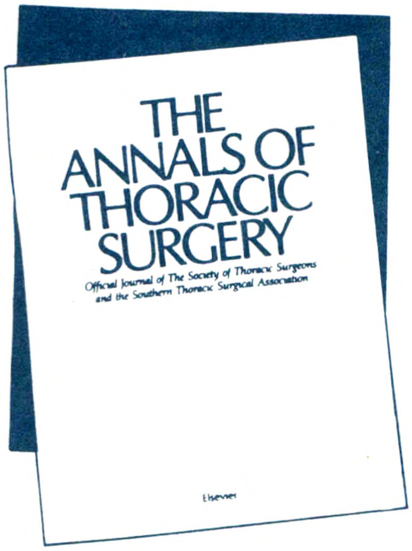
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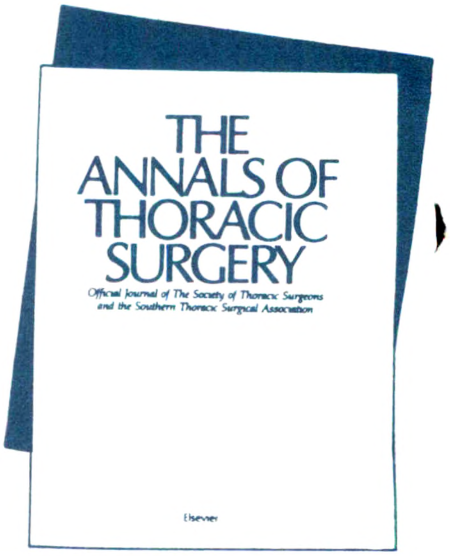

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Aortic Regurgitation After Left Ventricular Myotomy and Myectomy

Paul S. Brown, Jr, MD, Charles Stewart Roberts, MD, Charles L. McIntosh, MD, PhD, and Richard E. Clark, MD

Surgery Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

Five hundred twenty-five patients with hypertrophic cardiomyopathy underwent left ventricular myotomy and myectomy (LVMM) from 1960 to 1990. Four hundred ninety-six had nonregurgitant trileaflet aortic valves before LVMM. In 19 (4%) of these patients, aortic regurgitation developed after LVMM. Age of the 19 patients ranged from 10 to 58 years (mean age, 35 ± 3 years [± standard error of the mean]). Seven were male and 12, female. Five patients underwent LVMM followed immediately by aortic valve replacement or valvuloplasty. Aortic regurgitation developed in 14 patients at a later date. The average New York Heart Association functional class improved from 3.2 ± 0.1 to 1.3 ± 0.1 ($p < 0.05$, Student's t test) after operation. The average peak systolic left ventricular outflow tract gradient at rest and with provocation decreased from 65 ± 8 to 14 ± 5 mm Hg ($p < 0.05$) and 108 ± 9 to 45 ± 7 mm Hg ($p < 0.05$), respectively, 6 to 8 months after operation. Aortic regurgitation occurred in 7 of the 14 patients at 6 months or less after operation, and 3 required operative repair. In the other 7 patients, aortic regurgitation developed 3 years or more after LVMM, and 3 of them also required operative repair. All 12 patients in whom aortic regurgitation developed at operation or within 6 months postoperatively had either a very small aortic annulus (≤21 mm, 5 patients), a low mitral-septal contact lesion (≥35 mm below the aortic annulus, 3 patients), or both (4 patients). None of the patients in whom aortic regurgitation occurred 3 years or more postoperatively had an aortic annulus of 21 mm or less, and only 1 had a low mitral-septal contact point. A small aortic annulus or a low mitral-septal contact lesion greatly increased the difficulty of the operation and resulted in increased retraction of the aortic valve and annulus (with increased possibility of damage to the valve) to gain exposure to the interventricular septum. We recommend in patients with a very small aortic annulus, a low mitral-septal contact lesion, or both, that caution be exercised when operating through the aortic valve and that the valve be routinely evaluated postoperatively. If LVMM cannot be performed easily in these patients, consideration should be given to using another means of access to the interventricular septum or performing mitral valve replacement.

(Ann Thorac Surg 1991;51:585–92)

Operative treatment of hypertrophic cardiomyopathy (HC) was initiated in 1958 by Cleland, who performed the first transaortic left ventricular myotomy [1]. Since then, several methods to relieve left ventricular outflow tract obstruction have been developed and include ventricular septal myectomy by transaortic, atrial, and apical approaches in addition to mitral valve replacement and apicoaortic conduits. Transaortic left ventricular myotomy and myectomy (LVMM) has proved to be the most common operation employed to relieve left ventricular outflow tract obstruction. This approach, however, imposes the additional risk of postoperative aortic regurgitation (AR), which has been reported to occur in 5% to 54% of patients [2, 3]. This retrospective review of the 30-year experience at the National Heart, Lung, and Blood Institute (NHLBI) was undertaken to determine the incidence and cause of AR after LVMM.

Material and Methods

Patient Population

The database of the Surgery Branch of the NHLBI of the National Institutes of Health (NIH) was used to identify all patients with HC who underwent transaortic LVMM and had aortic valvular disease diagnosed preoperatively or postoperatively. Five hundred twenty-five patients underwent LVMM from 1960 to 1990. Fifteen of these patients had simultaneous LVMM and repair or replacement of a severely diseased aortic valve (5 with aortic stenosis, 6 with AR, and 4 with aortic stenosis and AR). Fourteen patients had 1+ to 2+ AR by preoperative cardiac catheterization, which did not require operative intervention. These 29 patients with preoperative aortic valvular disease were excluded.

The remaining 496 patients had nonregurgitant trileaflet aortic valves before LVMM. Aortic regurgitation has not developed in 477 (96%) of these patients, but in the remaining 19 (3.8%), it was noted at the time of LVMM (n = 5), 1 month to 6 months after operation (n = 7), or 3 years or more postoperatively (n = 7). This report focuses on these 19 patients who had normal aortic valves

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before operation but in whom AR subsequently developed.

The population of patients with HC at the NHLBI is unique in that there is 99% follow-up. All patients underwent preoperative cardiac catheterization, and surviving patients had postoperative cardiac catheterization at 6 months. The patients were routinely followed up in the outpatient clinic every 1 year to 2 years for life. A physical examination, chest radiograph, electrocardiogram, and echocardiogram were obtained at each clinic visit. All patients with any change in symptom complex or new echocardiographic findings underwent cardiac catheterization. If a patient missed a clinic appointment, he or she, the private physician, or both were contacted to find out the status of the patient. Outside cardiac catheterization results were entered into the database as was the cause of death or the autopsy results of any patient who died. At least 75% of the hearts of patients who died outside the NIH Clinical Center have been forwarded to the Pathology Branch, NHLBI, for examination. It is extremely unlikely that any of the 477 patients who were followed up for more than 5,000 patient-years have AR or died of AR without our knowledge.

Eighteen of the 19 patients in whom AR developed after LVMM underwent echocardiography or cardiac catheterization within 1 year of January 1, 1990, death, or both. The charts of and original operative notes for all 19 patients were reviewed, and the survivors underwent a physical examination. Total postoperative follow-up for these 19 patients was 214 patient-years (100% of potential follow-up) with a mean of 11 years per patient.

Operative Technique

All patients were operated on by one of two surgeons at the NHLBI. Three hundred fifty patients were operated on by Morrow [4] from 1960 to 1982 (8 were excluded from this review because of coexisting aortic valve disease), and 175 patients underwent operation by McIntosh [5, 6] from 1982 to 1990 (21 were excluded because of coexisting aortic valve disease). The indications for operation were New York Heart Association functional class III or IV symptoms refractory to medical management or a history of cardiac arrest.

The heart was exposed through a median sternotomy, the femoral artery was cannulated, a single venous cannula was passed into the right atrium, cardiopulmonary bypass was instituted, and a drainage cannula was passed through the left ventricular apex. Before 1982, flaccid anoxic arrest at 30°C was used; after that time, 26°C cardioplegic arrest with 4°C NIH oxygenated alkalotic crystalloid cardioplegia and iced slush were used. A vertical aortotomy was extended obliquely down to within 3 to 5 mm of the base of the center of the noncoronary sinus of Valsalva. Exposure of the septum was accomplished by anterior retraction of the right coronary leaflet with a cloth-covered retractor placed into the aortic root (Fig 1). A lighted, malleable ribbon retractor 18 to 24 mm wide was then placed through the aortic valve to protect the mitral apparatus (Fig 2). Additional septal exposure was achieved by counterpressure on the external surface of the right ventricle over the midportion of the septum with a stick sponge.

The first ventricular myotomy incision started 2 to 3 mm to the right of the midpoint of the right coronary leaflet. The second incision was placed 10 to 15 mm to the left of and parallel to the first incision, and the third incision was transverse and connected the previous two incisions. All of the incisions were continued at least 4 cm toward the ventricular apex with an attempt made to incorporate the fibrous plaque of mitral-septal contact into the area of resection (Fig 3). A single rectangular piece of muscle usually weighing between 1.5 and 3.0 g was removed. The aortic and mitral valves were carefully inspected for possible injury, and the aortotomy was closed. Diastolic blood flow of more than 1,000 mL/min through the left ventricular apex vent in the cold arrested heart was considered an indication for aortic valve replacement (AVR) or valvuloplasty at the same time as LVMM.

Before 1982, the three incisions were initiated at the aortic valve annulus; thereafter, they were started 5 to 10 mm below the annulus. This change was made because outflow obstruction usually does not occur above this point and because the ventricular septum frequently is thin in this basal area and thus predisposed to an increased risk of iatrogenic ventricular septal defect. In addition, it was thought that if the myectomy was started very close to the annulus, the aortic valve might lose structural support because of loss of tissue or as a result of gradual thickening and retracting of the scar. Support for the right coronary cusp was thought dependent on leaving the uppermost basal septum intact (Fig 4) [5].

Results

Preoperative and Postoperative Clinical Findings

Aortic regurgitation developed after LVMM in 19 (3.8%) of the 496 patients who had normal aortic valves preoperatively (Table 1). The ages of the 19 patients ranged from 10 to 58 years (mean age, 35 ± 3 years [± standard error of the mean]). Seven were male and 12, female. The ages of the 12 patients in whom AR developed at operation or 6 months or less postoperatively were significantly lower than those of the 7 patients in whom AR occurred 3 years or more after operation (mean age, 28 ± 3 years versus 48 ± 4 years; $p < 0.01$, Student's t test). Ten of the 12 patients who had AR within 6 months postoperatively were female compared with only 2 of the 7 patients with AR developing 3 years or more postoperatively. The average New York Heart Association functional class improved from 3.2 ± 0.1 to 1.3 ± 0.1 ($p < 0.05$) in all patients except 1 who did not survive LVMM (Table 2). The average resting peak systolic left ventricular outflow tract gradient decreased from 65 ± 8 to 14 ± 5 mm Hg ($p < 0.05$), and the average provoked peak systolic gradient decreased from 108 ± 9 to 45 ± 7 mm Hg ($p < 0.05$) (see Table 2). The preoperative and postoperative left ventricular outflow tract gradients, functional class, and cardiac indices were not significantly different from those in the previously published series on all of the patients who underwent LVMM at the NIH from 1960 through 1987 [4–6].

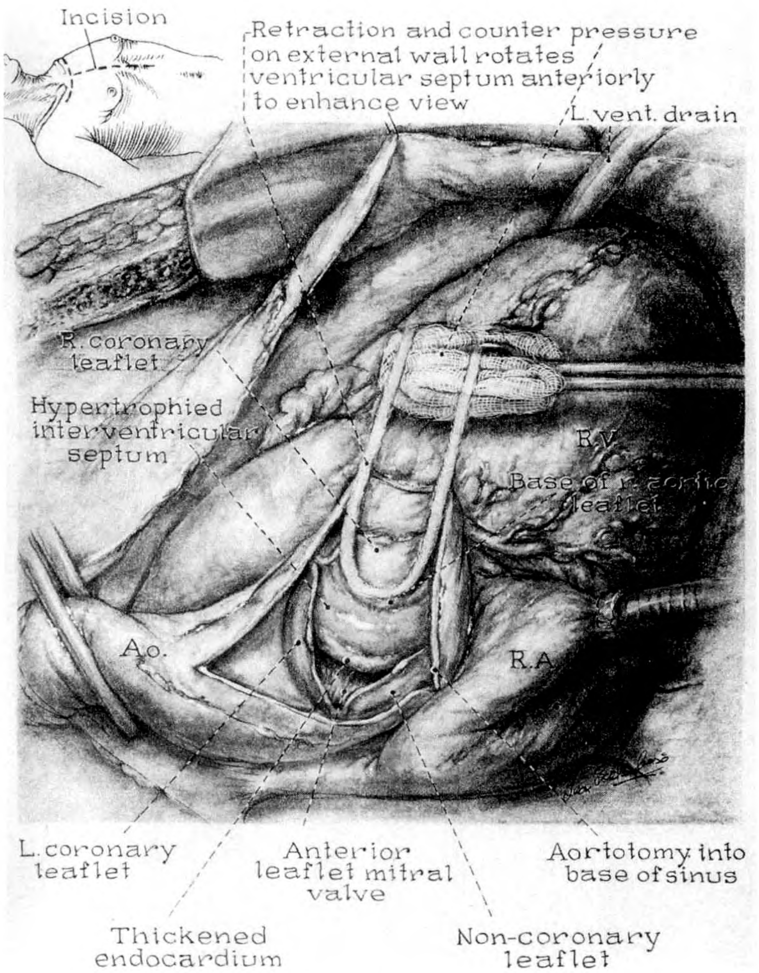
Incision
Retraction and counter pressure on external wall rotates ventricular septum anteriorly to enhance view
L. vent. drain
R. coronary leaflet
Hypertrophied interventricular septum
R.V.
Base of r. aortic leaflet
Ao.
R.A.
L. coronary leaflet
Anterior leaflet mitral valve
Aortotomy into base of sinus
Thickened endocardium
Non-coronary leaflet

Fig 1. Operative exposure of interventricular septum in preparation for left ventricular myotomy and myectomy. The bulging hypertrophied septum is visible below the right coronary leaflet, which is retracted anteriorly and to the left by the cloth-covered retractor. (Ao. = *aorta;* R.A. = *right atrium;* R.V. = *right ventricle.) (Reproduced with permission from Morrow AG. Hypertrophic subaortic stenosis. Operative methods to relieve left ventricular outflow obstruction. J Thorac Cardiovasc Surg 1978;76:423–30.)*

Aortic Regurgitation at Initial Operation

Five of the 19 patients underwent simultaneous LVMM and AVR or valvuloplasty. Three patients had tears of the aortic valve at the commissures between the noncoronary leaflet and the left or right leaflet and underwent primary repair. In 1 patient, the tear did not occur until the aortic cross-clamp was removed. In another patient, the valvuloplasty was not adequate after the aortic cross-clamp was removed, and AVR was performed. Valvuloplasty in these 3 patients was achieved by one or two 4-0 pledgeted Tevdek sutures at each torn commissure incorporating the adjacent leaflets.

The other 2 patients had severe AR after the aortic cross-clamp was removed and could not be weaned from cardiopulmonary bypass. There was no identifiable damage to the valve in either of these patients. One patient underwent AVR and the other, valvuloplasty. Valvuloplasty was performed in this patient because one of the leaflets originated several millimeters higher on the aortic wall than the others, and although it appeared normal when the aortic root was first opened, the leaflets did not coapt properly when the aortic root was opened the second time. Two 4-0 Tevdek sutures, incorporating adjacent leaflets, were placed at each commissure, with the overall result of lowering one leaflet and raising the origin of the two others on the aortic wall.

Two of the 3 patients who had only aortic valvuloplasty at initial operation required AVR 5 years and 11 years later.

Aortic Regurgitation Within 6 Months After Operation

Seven patients were diagnosed as having AR in the early postoperative interval (≤6 months). In 1 patient, AR developed at 1 week and in the others, it was found at the 6 months' postoperative cardiac catheterization. Two patients have been followed up for 1 year and 10 years without progression of 1+ AR. Aortic regurgitation was progressive in 5 patients, 3 of whom required an aortic procedure. The patient with AR at 1 week postoperatively died 16 years later of dilated cardiomyopathy with 4+ AR and 4+ mitral regurgitation. At postmortem examination, there was no evidence of any particular damage to the aortic valve, only redundant aortic leaflets, which did not coapt properly. One patient required valvuloplasty within 1 year postoperatively because of a tear of the suspension of the noncoronary and left coronary leaflets. The torn, prolapsed noncoronary leaflet was repaired by overlaying the leaflet with a triangular piece of pericardium sutured in place with 12 4-0 Prolene sutures. Two patients had AVR at 11 and 21 years after the initial operation because of progression of AR. At reoperation, they both had mildly thickened and retracted aortic leaflets. One patient

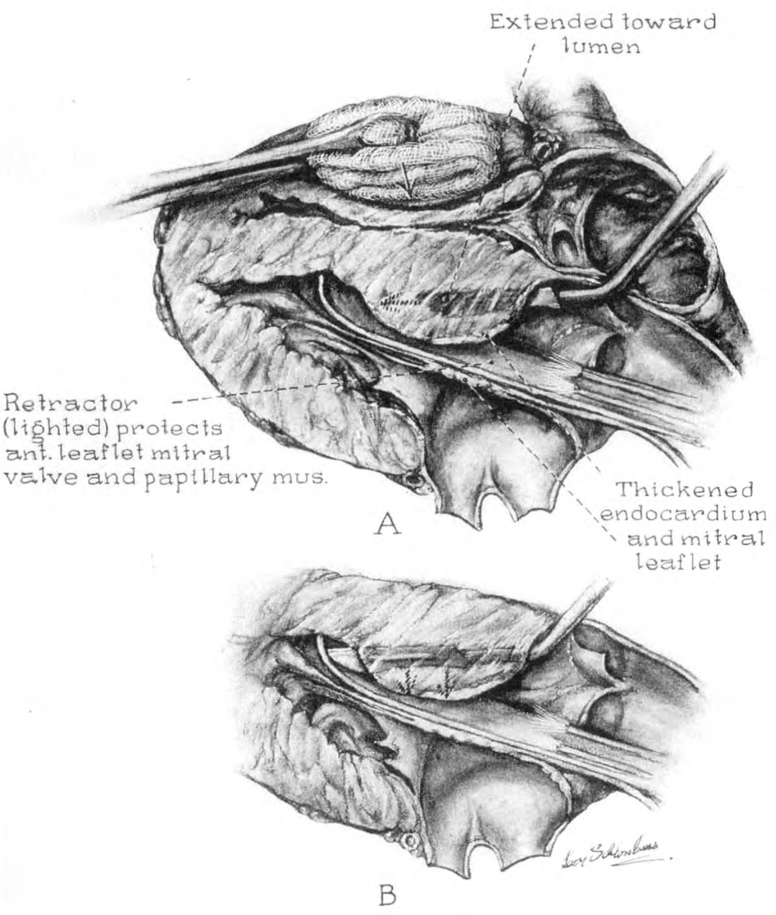
Extended toward lumen
Retractor (lighted) protects ant. leaflet mitral valve and papillary mus.
Thickened endocardium and mitral leaflet
A
B

Fig 2. A lighted ribbon retractor is passed through the aortic annulus toward the ventricular apex to protect the mitral apparatus. It is important not to stretch the aortic annulus, and an 18-mm ribbon retractor is usually sufficient. The knife blade is inserted into the septum parallel to the retractor for a distance of 4 cm. (Reproduced with permission from Morrow AG. Hypertrophic subaortic stenosis. Operative methods to relieve left ventricular outflow obstruction. J Thorac Cardiovasc Surg 1978;76:423–30.)

had a probable leaflet perforation diagnosed by aortogram, but has not required treatment to date.

Aortic Regurgitation 3 Years or More After Operation

Aortic regurgitation developed in 7 patients 3 years or more after operation. Three required AVR, and all 3 had minimally thickened and retracted leaflets at the time of AVR. A postmortem examination was done for 1 of the 2 patients who died before reoperation, and it showed no evidence of any particular aortic valve injury. However, the patient did have 3+ AR and 3+ mitral regurgitation. The other patient did not have an autopsy, but died of an

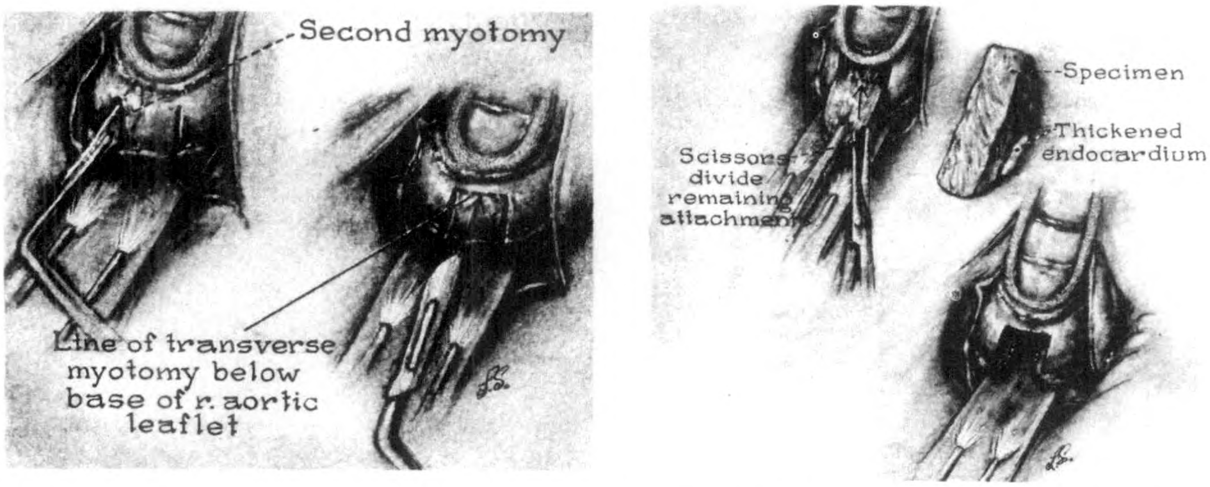
Second myotomy
Line of transverse myotomy below base of r. aortic leaflet
Specimen
Thickened endocardium
Scissors divide remaining attachment

Fig 3. Before 1982, the two vertical incisions were made at the aortic annulus and carried down toward the ventricular apex. (Reproduced with permission from Morrow AG. Hypertrophic subaortic stenosis. Operative methods to relieve left ventricular outflow obstruction. J Thorac Cardiovasc Surg 1978;76:423–30.)

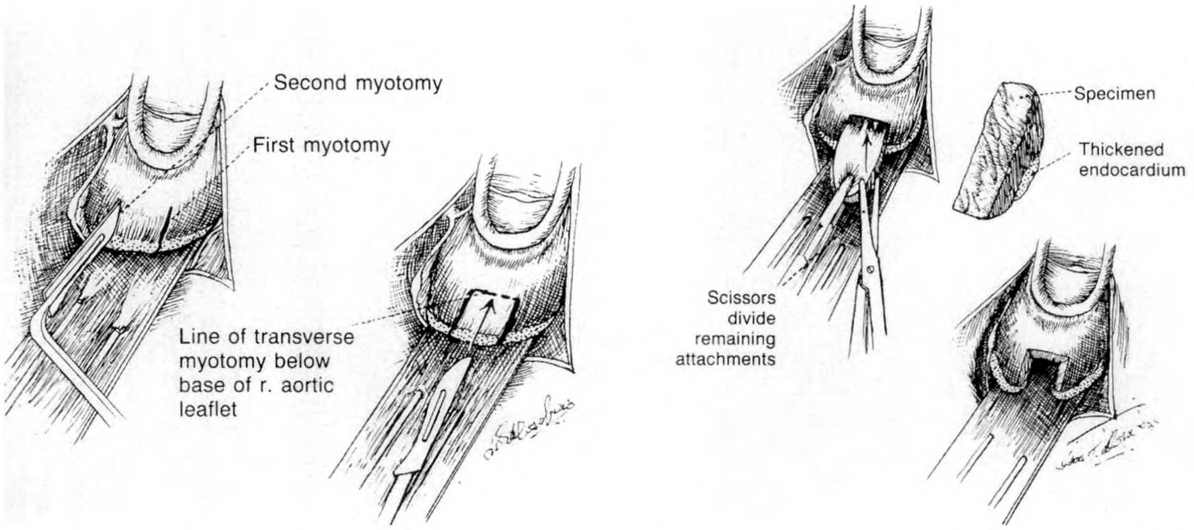
Second myotomy
First myotomy
Line of transverse myotomy below base of r. aortic leaflet
Scissors divide remaining attachments
Specimen
Thickened endocardium

Fig 4. After 1982, the two vertical incisions were made 5 to 10 mm below the aortic annulus. After completion of the resection, a rectangular channel 1 × 1.5 cm extends from the valve annulus toward the apex for about 4.5 cm. (Reproduced with permission from McIntosh CL. Idiopathic hypertrophic subaortic stenosis. In: Grillo HC, ed. Current therapy in cardiothoracic surgery. Toronto: B.C. Decker, 1989.)

arrhythmia at the NIH. Two patients also had a history of endocarditis/rheumatic fever; however, in each, the aortic valve appeared normal at the time of operation.

Comment

In this study, the incidence of AR after LVMM was 3.8% (19/496 patients). During LVMM, a considerable amount of force is applied to the aortic valve and annulus in opposite directions by retraction on the cloth-covered and lighted retractors to visualize the interventricular septum. Several conditions exist whereby more retraction than usual is required to deliver the septum into the outflow tract. Septal hypertrophy that was to the right or left of the 12-o'clock position when looking down through the aortic valve (2 patients), a very small aortic annulus (9 patients), and a low mitral-septal contact lesion (7 patients) substantially increased the difficulty of the operation and resulted in a greater amount of retraction necessary on the aortic valve.

All 12 patients in whom AR developed at operation or within 6 months postoperatively had a very small aortic annulus (≤21 mm, 5 female patients), a low mitral-septal contact lesion (≥35 mm below the aortic annulus, 3 patients), or both (4 female patients). None of the patients in whom AR developed more than 6 months postoperatively had an aortic annulus 21 mm or smaller, and only 1 patient had a mitral-septal contact point 35 mm or more below the aortic annulus. Postoperative AR also occurred after an LVMM performed simultaneously through the aortic valve and left ventricular apex (1 patient) and after the removal of 11.4 g of septal tissue (the usual amount of septal tissue removed was 1.5 to 4.0 g).

The patients with postoperative AR fell into two groups. The first group was composed of patients with AR occurring at operation or within 6 months after operation. The mean age was 28 years, which is significantly lower ($p < 0.01$) than that of all patients who underwent LVMM (mean age, 35 years) and that of patients in whom AR developed 3 years or more postoperatively (mean age, 48 years; $p < 0.01$, Student's t test). Ten of the 12 were female (83% versus 44% in the entire group of patients undergoing LVMM), and 5 of the 12 had tears of the aortic valve. The second group comprised 7 patients (5 male) in whom AR developed 3 to 14 years after LVMM. This group was significantly older, the mean age being 48 years at LVMM and 55 years at the time AR occurred. None of those who underwent AVR had identifiable tears in the aortic valve. The population of all patients who underwent LVMM was 54% male (mean age, 43 years) and 46% female (mean age, 48 years).

Iatrogenic damage to the aortic valve or injury to the annulus occurs immediately or within the first 6 months after LVMM and is more likely to occur in patients with a small aortic valve annulus (young female patients) or patients with a low mitral-septal contact lesion. It is hard to attribute AR occurring 3 years or more after LVMM to the operation itself, especially as only 1 patient had a low contact lesion and none had a small aortic annulus. The development of AR more than 3 years after LVMM may represent a stretch injury to the valve, but most likely represents the development of aortic valvular disease unrelated to LVMM.

The operative mortality rate (death occurring < 30 days after operation or before discharge) in the series of patients seen from 1960 to 1982 was 8% [6] with a 5-year mortality rate of 9% and a 10-year mortality rate of 27% (excluding operative deaths) from causes attributable to HC [5]. Eight of the late deaths were thought to be due to arrhythmia and 9, end-stage HC (8 patients had ≥ 3+ mitral regurgitation); the rest followed or were a consequence of further operation or failure of prosthetic valves.

Table 1. Summary of Data on 19 Patients in Whom Aortic Regurgitation Developed at or After Operation

Patient No.	Age (y)	Sex	AV Annulus ≤21 mm	Contact Lesion ≥35 mm	LVMM Begun at AV	Initial Operation	AR at 6-Month Postop Catheterization	Time of Discovery of AR[a]		Cause of AR	Time to Second Operation		Type of Second Operation	Total Follow-up				Cause of Death
								Time	AR		Years	AR		Years	AR	Status	FC	
AR At LVMM																		
1	22	F	Yes[b]	Yes	No	AVR	. . .	Operation		NSE	. . .		. . .	0	. . .	Dead	. . .	MSOF 1 wk postop, in hospital
2	44	F	Yes	No	No	AVP, AVR	0+	Operation		Tear	. . .		. . .	8	0+	Alive	II	. . .
3	17	F	Yes	No	Yes	AVP	1+	Operation and 6 mo	1+	Tear	. . .		. . .	9	1+	Alive	I	. . .
4	21	F	Yes	No	Yes	AVP	3+	Operation and 6 mo	3+	Tear	5	4+	AVR	5	0+	Dead	. . .	MSOF 1 d postop, in hospital
5	22	M	No	Yes	Yes	AVP	0+	Operation and 9 y	2+	NSE	11	4+	AVR	14	0+	Alive	II	. . .
AR ≤6 Months After LVMM																		
6	10	M	No	Yes	Yes	. . .	1+	1 wk	1+	?	. . .		. . .	16	4+	Dead	. . .	Dilated cardiomyopathy (4+ MR)
7	25	F	Yes	No	Yes	. . .	1+	6 mo	1+	?	. . .		. . .	10	1+	Alive	I	. . .
8	35	F	Yes	No	Yes	. . .	1+	6 mo	1+	NSE	11	3+	AVR	25	0+	Alive	I	. . .
9[c]	38	F	Yes	Yes	Yes	. . .	1+	6 mo	1+	NSE	21	4+	AVR	27	0+	Dead	. . .	MSOF 2 mo after MVR, in hospital
10	44	F	Yes	Yes	No	. . .	1+	6 mo	1+	?	. . .		. . .	1	1+	Alive	II	. . .
11	24	F	No	Yes	Yes	. . .	2+	6 mo	2+	Tear	. . .		. . .	8	3+	Alive	I	. . .
12	35	F	Yes	Yes	No	. . .	2+	6 mo	2+	Tear	<1	3+	AVP	2	0+	Alive	II	. . .
AR ≥3 Years After LVMM																		
13	38	M	No	Yes	Yes	. . .	0+	3 y	1+	?	. . .		. . .	12	2+	Dead	. . .	Arrhythmia, in hospital
14	58	M	No	No	No	. . .	0+	3 y	1+	?	. . .		. . .	4	1+	Alive	II	. . .
15	57	F	No	No	Yes	. . .	0+	3 y	2+	NSE	11	3+	AVR	14	0+	Alive	II	. . .
16	58	M	No	No	No	. . .	0+	3 y	2+	?	. . .		. . .	3	2+	Alive	II	. . .
17[d]	36	M	No	No	Yes	. . .	0+	11 y	2+	NSE	15	3+	AVR	25	0+	Dead	. . .	Arrhythmia
18	46	F	No	No	Yes	. . .	0+	11 y	2+	NSE	12	3+	AVR	12	0+	Dead	. . .	MSOF 3 d after MVR, in hospital
19	44	M	No	No	Yes	. . .	0+	14 y	3+	?	. . .		. . .	16	3+	Dead	. . .	Dilated cardiomyopathy (3+ MR)

[a] Murmur, cardiac catheterization, or echocardiographic evidence of AR with subsequent aortogram. [b] This patient was barely able to have a 17-mm Björk-Shiley aortic valve implanted. [c] This patient underwent repeat LVMM 5 years after this operation without change in degree of AR. [d] The case of this patient was described in a case report by Wiener and colleagues [7].

AR = aortic regurgitation; AV = aortic valve; AVP = aortic valvuloplasty; AVR = aortic valve replacement; FC = functional class (New York Heart Association); LVMM = left ventricular myotomy and myectomy; MR = mitral regurgitation; MSOF = multisystem organ failure; MVR = mitral valve replacement; NSE = no specific etiology determined after examination of aortic valve; tear = tear in leaflet.

Table 2. Summary of Hemodynamic Data on the 19 Patients

Patient No.	Preop Catheterization				6-Month Postop Catheterization				
		LV-AO Gradients[a]				LV-AO Gradients[a]			
	FC	Resting	Provoked	CI	FC	Resting	Provoked	CI	AR (0–4)
AR at LVMM									
1	III	50	80	2.1	. . .	. . .	. . .	. . .	. . .
2	III	58	106	2.6	II	0	50	2.5	0+
3	III	40	100	2.7	I	15	30	2.8	1+
4	II	20	40	3.0	I	0	25	2.8	3+
5	IV	115	135	3.7	I	0	40	3.0	0+
AR ≤6 Months After LVMM									
6	III	60	100	2.7	I	40	50	2.9	1+
7	IV	67	100	2.2	I	50	88	2.4	1+
8	III	42	130	1.4	I	30	100	2.0	1+
9	III	110	. . .	3.0	II	0	30	3.0	1+
10	III	107	. . .	2.6	I	80	. . .	2.1	1+
11	III	100	. . .	2.5	I	0	0	3.3	2+
12	IV	100	. . .	2.8	III	0	52	2.5	2+
AR ≥3 Years After LVMM									
13	III	60	90	3.6	II	15	20	3.5	0+
14	III	33	150	2.6	I	0	20	2.4	0+
15	III	0	100	1.9	I	0	0	2.9	0+
16	IV	18	70	2.0	I	8	60	2.6	0+
17[b]	III	68	115	2.9	I	15	65	2.1	0+
18	III	137	. . .	2.4	II	0	55	3.7	0+
19	IV	48	190	1.8	I	0	85	2.0	0+
Mean ± SEM	3.2 ± 0.1	65 ± 8	108 ± 9	2.6 ± 0.6	1.3 ± 0.1	14 ± 5	45 ± 7	2.7 ± 0.1	

[a] Highest provocable gradient was measured during Valsalva maneuver, inhalation of amyl nitrite, or infusion of isoproterenol. [b] The case of this patient was described in a case report by Wiener and colleagues [7].

AO = aortic pressure (mm Hg); AR = aortic regurgitation; CI = cardiac index ($L \cdot min^{-1} \cdot m^{-2}$); FC = functional class (New York Heart Association); LV = left ventricular pressure (mm Hg); LVMM = left ventricular myotomy and myectomy; SEM = standard error of the mean.

The operative mortality rate in the patients seen from 1982 to 1990 was significantly lower at 3% ($p < 0.05$, Student's t test) with an unchanged 5-year mortality rate of 8% (excluding operative deaths). Three of the late deaths were attributable to arrhythmia, 1 was due to end-stage HC, and the rest were attributable to other cardiac operations or valve failure.

A review of four other large series of patients with HC who underwent LVMM shows that AR requiring AVR is rare; however, the incidence of mild to moderate AR is possibly much higher than previously recognized. Sasson and associates (Toronto General Hospital) [3] reported that mild to moderate AR as measured by Doppler echocardiography developed postoperatively in 28 (54%) of 52 patients. Six (12%) had a murmur of AR, and only 1 patient underwent a second operation. The patient who underwent reoperation, as in the current series, was noted to have a somewhat thickened and deformed aortic valve. The discrepancy between the 54% incidence of AR by Doppler echocardiography and our 3.8% incidence by cardiac catheterization remains unexplained, though perhaps Doppler echocardiography picks up too many cases of trivial AR possibly unrelated to LVMM. Turina and co-workers (Zurich, Switzerland) [8] reviewed the late echocardiographic findings in 59 patients who had a transaortic LVMM. Regurgitation developed in 4 patients (7%) more than 8 years after initial operation, and none required reoperation. Mohr and associates (Mayo Clinic) [2] described the occurrence of postoperative AR in 6 (5%) of 111 patients, 3 of whom later required AVR, and Krajcer and colleagues (Texas Heart Institute) [9] reported on 127 patients who underwent LVMM; there was no mention of AR as a postoperative complication.

The incidence of AR after LVMM is low and should not be considered a contraindication to a transaortic approach. However, AR is not well tolerated in patients with HC, as they are generally sensitive to increases in left ventricular end-diastolic pressure and volume because of poor compliance, even though the hypertrophic ventricle generally protects against the development of ventricular dilatation. An aortic valve size of 21 mm or less is small by any standard, and in our experience, a valve of this size or a low mitral-septal contact lesion was a rare finding. Only 4 of the last 100 patients undergoing LVMM had an aortic root 21 mm or smaller by echocardiography, 3 of whom are included in this report. There were certainly some patients with a small aortic annulus and a low contact lesion in whom AR did not develop; however, it is remarkable that all of the patients with early postoperative AR had one of these two findings.

We recommend continuing the practice of making the septal incisions 5 to 10 mm below the aortic valve annulus because it makes sense not to incise the thinnest portion of the septum when obstruction does not take place at that point. We note, however, that no significant change in the incidence of AR occurred after the modification in operative technique; AR developed in 3.8% (13/342) of patients before 1982 and 3.9% (6/154) after 1982. When patients with an aortic annulus sized 21 mm or smaller, a low mitral-septal contact lesion 35 mm or more from the aortic valve, or both of these conditions undergo transaortic LVMM, one must be especially cognizant of possible injury to the aortic valve or annulus, which in our experience has not been very amenable to repair (3 of 5 patients who underwent valvuloplasty have required AVR, and the other 2 patients have been followed up for 9 years and less than 1 year). If LVMM cannot be performed in these patients, consideration should be given to using another approach to the interventricular septum or performing mitral valve replacement. Finally, the patients should be carefully followed up for the presence of postoperative AR for at least 6 months, which could be a cause of further continued symptoms and eventually require operative intervention.

References

1. Cleland WP. The surgical management of obstructive cardiomyopathy. J Cardiovasc Surg (Torino) 1963;4:489–91.
2. Mohr R, Schaff HV, Danielson GK, Puga FJ, Pluth JR, Tajik J. The outcome of surgical treatment of hypertrophic obstructive cardiomyopathy. J Thorac Cardiovasc Surg 1989;97:666–74.
3. Sasson Z, Prieur T, Skrobik Y, et al. Aortic regurgitation: a common complication after surgery for hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol 1989;13:63–7.
4. Morrow AG. Hypertrophic subaortic stenosis: operative methods utilized to relieve left ventricular outflow obstruction. J Thorac Cardiovasc Surg 1978;76:423–30.
5. McIntosh CL. Idiopathic hypertrophic subaortic stenosis. In: Grillo HC, ed. Current therapy in cardiothoracic surgery. Philadelphia, Toronto: B.C. Decker, 1989:391–7.
6. McIntosh CL, Maron BJ. Current operative treatment of obstructive hypertrophic cardiomyopathy. Circulation 1988;78:487–95.
7. Wiener MW, Vondoenhoff LJ, Cohen J. Aortic regurgitation first appearing 12 years after successful septal myectomy for hypertrophic obstructive cardiomyopathy. Am J Med 1982;72:157–60.
8. Turina J, Jenni R, Krayenbuehl HP, Turina M, Rothlin M. Echocardiographic findings late after myectomy in hypertrophic obstructive cardiomyopathy. Eur Heart J 1986;7:68–92.
9. Krajcer Z, Leachman RD, Cooley DA, Coronado R. Septal myotomy myomectomy versus mitral valve replacement in hypertrophic cardiomyopathy. Circulation 1989;80(Suppl 1):57–64.

Tricuspid Valve Repair for Tricuspid Valve Endocarditis: Tricuspid Valve "Recycling"

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Tricuspid valve endocarditis traditionally has been treated with either valve excision or valve replacement. To avoid implantation of foreign material in an infected field, we have applied the principles of mitral valve repair to 4 patients with tricuspid valve endocarditis. On preoperative echocardiography, all patients had 3 to 4+ tricuspid regurgitation, evidence of progressive right ventricular enlargement, and mobile vegetations. In each case, up to three quarters of the anterior leaflet was excised en bloc with infected chordae and papillary muscle heads. Surgical procedures included standard quadrangular resection, conversion to a bicuspid valve, and pericardial patch replacement of the anterior leaflet with mobilization of basal chordae to replace resected marginal chordae. On postoperative echocardiography, tricuspid regurgitation and right ventricular dimensions were reduced in 2 of 4 patients in spite of loss of leaflet tissue. All excised valve tissue demonstrated bacteria on Gram stain or culture. Nonetheless, all repaired valves were successfully sterilized without recurrent infections. Tricuspid valve repair can allow eradication of infection with potential for improving valve competency in complicated tricuspid valve endocarditis.

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The correct surgical treatment for tricuspid valve endocarditis remains an item of debate. Of the two procedures commonly practiced, namely, tricuspid valve excision and tricuspid valve prosthetic replacement, both options have serious drawbacks. Patients with tricuspid valve excision must tolerate florid tricuspid regurgitation and 20% of these patients require valve replacement. Patients who undergo initial tricuspid valve replacement in the face of acute infection are at risk for recurrent endocarditis as the prosthetic valve must be implanted in an infected field. Also, among the population of intravenous drug abusers, later episodes of endocarditis due to reinfection of the prosthesis must be expected.

In an effort to provide an alternative surgical choice for this clinical problem, a program of tricuspid valve repair was initiated as primary treatment for cases of tricuspid valve endocarditis requiring operation. To accomplish this end, the principles of mitral valve repair have been applied to the tricuspid valve and some innovations to standard mitral valve techniques have been added.

Methods and Results

Four patients were accepted for surgical reconstructive therapy for tricuspid valve endocarditis.

Indications for Operation

Among these 4 patients, the cause of endocarditis was intravenous drug abuse in 2 patients. The other 2 patients had histories of recent dental abscesses. All patients had at least two indications for operation. Recurrent septic pulmonary emboli were present in all 4 patients. One patient was carried through a pregnancy to term on antibiotic therapy and referred for surgical treatment when recurrent pulmonary emboli developed after completion of a 1-month course of antibiotics. In addition, 2 patients had unresolved sepsis after 3- and 4-week courses of antibiotics, respectively. Two patients had echocardiographic evidence of flail leaflets, and 2 had progressive right ventricular dilatation on serial echocardiograms.

Preoperative Echocardiographic Results

On preoperative echocardiography, all patients had moderate to severe (3 to 4+) tricuspid regurgitation, evidence of right ventricular volume overload, and visible vegetations. Vegetations were all greater than 1 cm in diameter and frequently pedunculated, prolapsing across the plane of the tricuspid valve annulus into the right atrium. One patient had a flail anterior leaflet with an attached mobile vegetation and a second sessile vegetation evident in the apex of the right ventricle. No patient had evidence of left-sided valve involvement.

Bacteriological Results

Bacteriological data are chronicled in Table 1. Two patients had blood cultures positive for multiple organisms. At operation, all vegetations were submitted for Gram stain, histology, and a routine battery of cultures. With all patients on antibiotic therapy at the time of operation, excised valve tissue yielded positive Gram stain for bacteria in 3 of 4 patients; histology confirmed the presence of gram-positive cocci in 3 of 4 patients. However, only 1 patient had a positive tissue culture. In this case, culture

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Table 1. Bacteriological, Echocardiographic, and Operative Data

Patient No.	Cause	Bacteriology		Preop Echo	Postop Echo	Resection	Repair
		Blood Cultures	OR Cultures				
1	Dental abscess	*Streptococcus muelleri*	Gram stain: gram-positive cocci Histology: gram-positive cocci Culture: –	3+ TR, increasing RV size, 2-cm vegetation increasing in size, flail leaflet	3+ TR, RV mildly dilated	Posterior half of anterior leaflet with chordae	Bicuspidization, localized annuloplasty
2	Dental abscess	*Haemophilus parainfluenzae, Streptococcus anginosus-constellatus, Streptococcus salivarius, Bacteroides intermedius*	Gram stain: gram-positive cocci Histology: gram-positive cocci Culture: –	3+ TR, increasing RV size, 2-cm vegetation	3+ TR, RV mildly dilated	Central 3/4 of anterior leaflet, chordae, tip of papillary muscle	Primary leaflet repair, localized annuloplasty
3	IV drug abuse	*Staphylococcus aureus, Streptococcus viridans, Haemophilus parainfluenzae*	Gram stain: – Histology: – Culture: + *Staphylococcus epidermidis*	3+ TR, 2 vegetations (1 cm & 1.7 cm), RV dilated	1+ TR, decreased RV dilatation	Central half of anterior leaflet with 3 chordae	Primary leaflet repair, localized annuloplasty, Carpentier-Edwards ring
4	IV drug abuse	*Staphylococcus aureus*	Gram stain: gram-negative rods Histology: gram-positive cocci Culture: –	4+ TR, dilated TV annulus, 2–3-cm vegetation, RV dilatation, flail leaflet	1+ TR (late postop: 3+), decreased TV annular size, decreased RV dilatation	Central 3/4 of anterior leaflet, ruptured chordae, papillary muscle head	Pericardial patch, mobilized basal chordae, DeVega annuloplasty

IV = intravenous; OR = operating room; RV = right ventricular; TR = tricuspid regurgitation.

of the excised vegetation at operation revealed a different organism than previous positive blood cultures. This was believed to represent a partially treated polymicrobial infection or an interim secondary infection of a necrotic vegetation by a resistant organism rather than a surgical contaminant.

Operative Findings and Surgical Approach

The operative approach was through a standard median sternotomy incision. Bicaval cannulas with caval tapes were used for venous drainage. Dependent pump suction near the coronary sinus in the right atrium was the most effective means of providing a blood-free field for visualization of the valve apparatus. Three patients underwent valve repair under aortic cross-clamp with hypothermic arrest using cold crystalloid cardioplegia; in 1 acutely septic patient, repair was accomplished without aortic occlusion, with the heart beating under normothermic conditions. In all patients, valve function was assessed intraoperatively both before and after repair under normothermic conditions with the heart beating. Intraoperative transesophageal echocardiography was used in the 2 most recent patients to evaluate the surgical repair. There was no perioperative mortality.

On intraoperative inspection, all 4 patients were found to have involvement of the anterior leaflet of the tricuspid valve. In all patients, the infectious process affected the leaflet tissue and free margin with associated chordae and papillary muscles. The infection extended up to the annulus in all patients, but there was no direct annular involvement or evidence of annular abscess in any of the 4 patients. Because the repair procedures were all performed in contaminated fields, monofilament sutures were used exclusively and pledgets were constructed of pericardium, avoiding Teflon felt or other prosthetic material.

In 2 patients, the central one half to three quarters of the anterior leaflet was excised along with infected chordae. The leaflet margins were reapproximated with 5-0 Prolene suture (Ethicon, Somerville, NJ) and a localized annuloplasty or annular plication was performed with 3-0 Prolene suture using pericardial pledgets (Fig 1). In 1 such

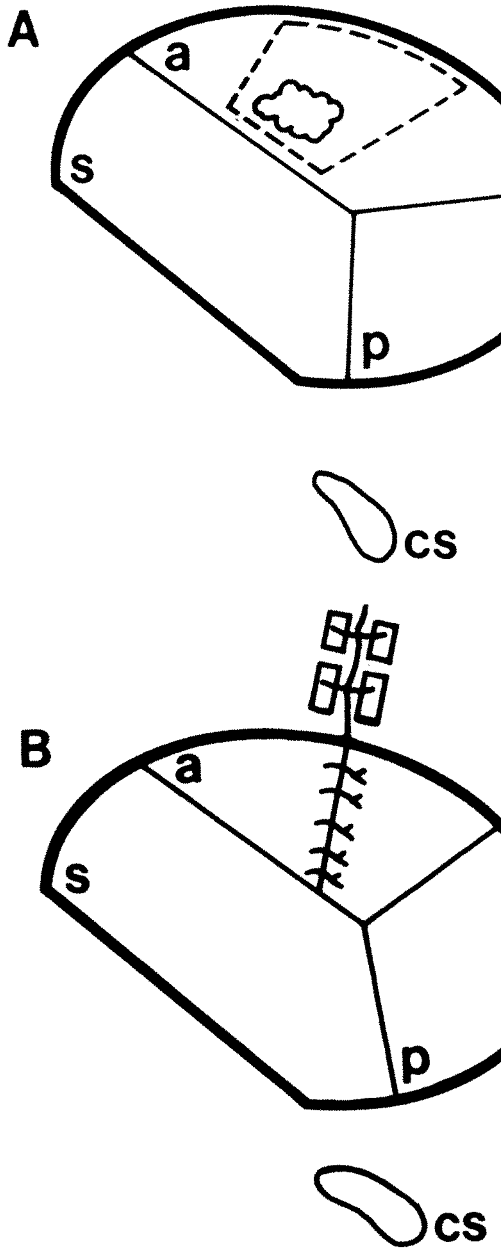

*Fig 1. (A) One half to three quarters of the anterior leaflet of the tricuspid valve and attached chordae were excised with a quadrangular resection. (B) An annuloplasty was performed using pericardial pledgets. The leaflet margins were approximated with 5-0 Prolene suture. (*a *= anterior leaflet;* cs *= coronary sinus;* p *= posterior leaflets;* s *= septal leaflet.)*

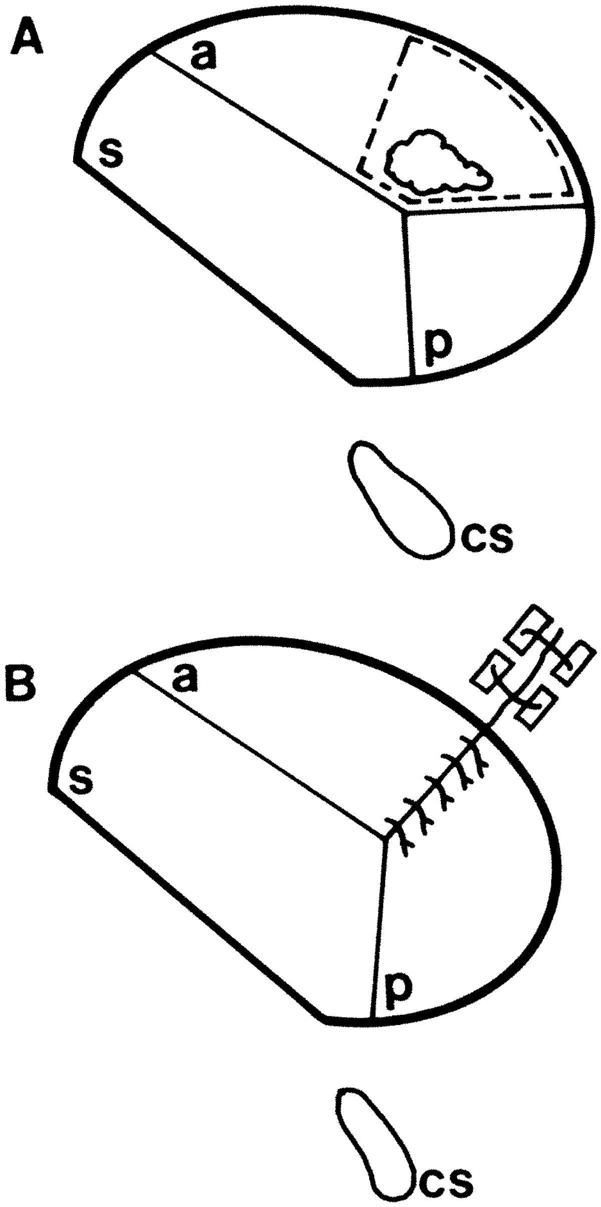

Fig 2. (A) The posterior half of the anterior leaflet of the tricuspid valve was excised with involved chordae. (B) Annuloplasty was performed. The remaining anterior leaflet was sutured to the intact posterior leaflet. (Abbreviations as in Figure 1.)

patient who had completed a course of antibiotics, a Carpentier-Edwards annuloplasty ring was added to provide valve competence. In another patient, excision of the posterior half of the anterior leaflet produced a defect that could not be closed and the anterior half of the leaflet was sutured to the posterior leaflet after annular plication, producing a bicuspid valve (Fig 2).

In the most recent patient, extensive excision of the anterior leaflet left only a rim of tissue on the margins of the leaflet and the leaflet could not be primarily reapproximated. Also, the presence of an infected papillary muscle necessitated excision of the papillary muscle head as well as excision of all attendant chordae, thus leaving no suspension for the valve leaflet. In this situation, a half circle of pericardium was fashioned to serve as a new anterior leaflet. Basilar chordae were mobilized and dissected down from the right ventricular wall, using their muscular trabecular attachments to form new, potentially contractile papillary muscles. The constructed "chordae" were affixed to the free pericardial margins to form a functioning leaflet (Fig 3). This reconstructed valve was competent on intraoperative testing and on transesoph-

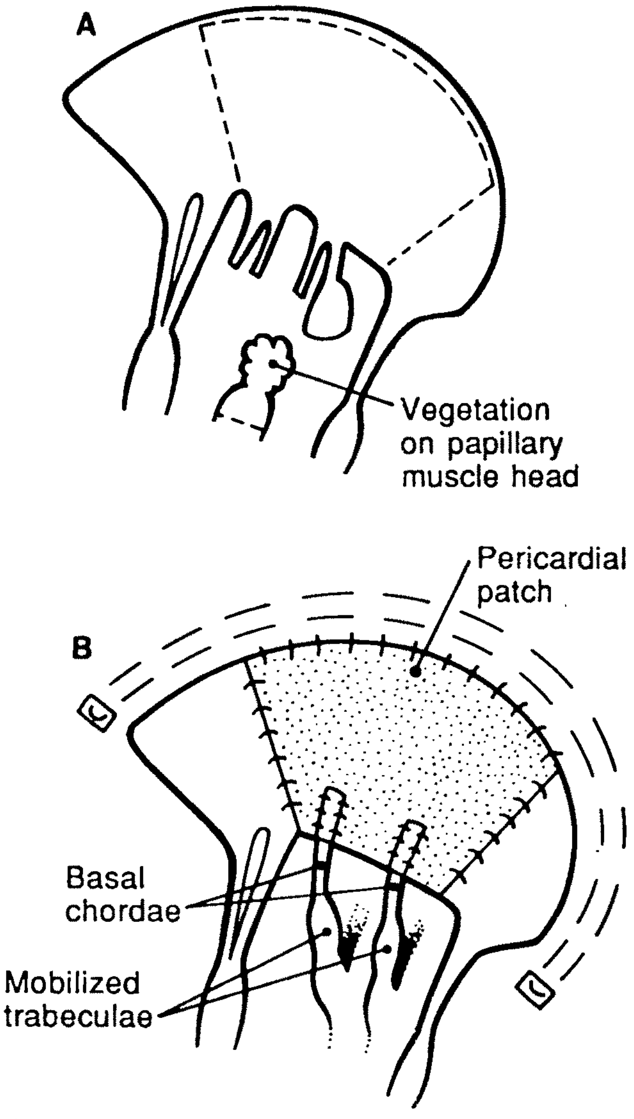

Fig 3. (A) (Anterior leaflet only depicted.) Three quarters of the central portion of the anterior tricuspid leaflet was excised along with vegetations and two sets of ruptured chordae. An infected papillary muscle head was also excised. (B) A trapezoidal patch of pericardium was sutured in replacement for the central portion of the anterior leaflet. Uninfected basal chordae inserting near the annulus were detached and mobilized by dissecting the attached trabeculae off the right ventricular wall. These mobilized "substitute chordae" were then fixed to the free margin of the pericardial leaflet. A DeVega-type annuloplasty was performed.

ageal echocardiography after coming off bypass. However, in the weeks to months after operation the valve became less competent, probably secondary to recurrence of annular dilatation.

Postoperative Echocardiography

Echocardiography performed after repair revealed diminished tricuspid regurgitation in 2 of 4 patients but late persistence of tricuspid regurgitation in 3 of 4. Only mild tricuspid regurgitation was noted in the 1 patient in whom the Carpentier-Edwards annuloplasty ring was added. No patient had tricuspid stenosis secondary to reduction of annular dimensions. In 2 of 4 patients, right ventricular dilatation was clearly reduced compared with the preoperative echocardiogram, and in the other 2 the right ventricle was only mildly dilated postoperatively. Only 1 patient had symptoms or signs of right heart failure postoperatively, and this was managed with diuretics.

Bacteriologic Follow-up

All patients completed full courses of antibiotics for 2 to 6 weeks postoperatively. The single patient whose culture grew different bacteria than on preoperative blood culture underwent a full 6-week course of antibiotics appropriate for the new organism. There was no evidence of recurrent endocarditis, extension of the valvar infection to other valves or into the surrounding myocardium, or evidence of new septic emboli in any of the patients.

Comment

Of the 4 patients studied, 2 were found to have infections due to multiple organisms. In a recent review of tricuspid valve endocarditis, Chan and associates [1] report an increased frequency of polymicrobial infections in the tricuspid position.

The pattern of valve involvement by the infectious process in this group of patients is strikingly similar in all 4 cases in spite of the different bacteriology. The anterior leaflet was affected in all cases and, on the anterior leaflet, the process involved the leaflet margin, chordae, and papillary muscles but spared the annulus. Valve repair was possible because the annulus and surrounding myocardium were not grossly infected.

The anterior leaflet of the tricuspid valve may be primarily involved because of its position across the right ventricular inflow tract, perhaps exposing it to bloodborne bacteria to a greater degree than other leaflets. The propensity for involvement of the free margin and absence of annular involvement is different from the anatomical problems encountered with mitral valve or aortic valve endocarditis. Local factors, such as differences in the blood supply to the annular area and surrounding myocardium, may account for the various manifestations of endocarditis among different valve positions. Alternatively, one might postulate that all endocarditides may involve the free margin first and spread secondarily to the annulus. In the tricuspid valve, septic pulmonary emboli may provide early symptoms of endocarditis, leading to diagnosis at an earlier stage in the infectious process, before annular and myocardial invasion.

Supporting the latter hypothesis are at least 4 reported cases in which tricuspid valve endocarditis was treated successfully with excision of a vegetation alone [2–5]. Thus, excision of a vegetation might be potentially curative in a majority of cases of tricuspid endocarditis if performed early in the course, before the development of leaflet destruction.

Current surgical options for the treatment of more involved tricuspid valve endocarditis with leaflet destruction entail certain disadvantages. Tricuspid valve excision results in severe tricuspid regurgitation, which may not be well tolerated in 18% to 30% of patients [1, 6, 7]. Of 61 patients with tricuspid valve excision reported by Arbulu and Asfaw [6], the 60-day perioperative mortality was 10%; 18% of patients required later prosthetic tricuspid valve insertion, and 10% of the remaining surviving patients had symptoms and signs of heart failure. The fact that this operation succeeds in even 80% of patients as a standard of care reflects the composition of the patient population—young intravenous drug abusers with previously healthy hearts and frequently normal pulmonary vascular resistances. However, in this group of patients, pulmonary hypertension may also be present immediately, secondary to multiple pulmonary emboli, or develop later, and this situation may result in progressive right heart failure with an absent tricuspid valve.

Implantation of a prosthetic valve in an infected field risks reinfection. Of 10 patients who underwent immediate bioprosthetic valve replacement reported by Stern and associates [8], all survived to hospital discharge, but resumption of intravenous drug abuse led to death due to sepsis in 3. One patient required valve re-replacement for recurrent endocarditis. In this frequently young patient population, calcification of bioprosthetic valves may necessitate reoperation within a decade. Mechanical valves entail anticoagulation, which may be difficult to achieve in a noncompliant patient group.

The best immediate or short-term solution to the problem of tricuspid valve endocarditis would be reconstruction of the native valve without prosthetic material. Especially with the propensity to reinfection with continuing intravenous drug abuse, the elimination of prosthetic materials might allow antibiotic treatment of future episodes of endocarditis. To this end, a program was initiated at this institution to repair the tricuspid valve as a first step in the surgical therapy of tricuspid valve endocarditis. The principles elaborated by Carpentier [9] were employed and expanded upon to address special situations encountered in tricuspid valve anatomy. The use of trabeculae and basal chordae attached to functioning myocardium to provide semifunctional chordae to a pericardial leaflet is a new approach with applications yet unproven.

In the mitral position, one has the option of translocating or transferring a chordal group from the directly opposed leaflet margin to the reconstructed leaflet. Because the chordae serving the three leaflets in the tricuspid valve are not directly opposite one another, this solution may be less attractive in the tricuspid position. Nonetheless, chordal transposition was used successfully by Dreyfus and co-workers [10] in 5 tricuspid valve repair procedures in which concomitant extensive resections were apparently not required. The chordae to the septal leaflet are not always expendable. As the posterior leaflet of the tricuspid valve can be completely excluded, chordae to the posterior leaflet could be used for chordal transposition. However, in patient 4, posterior leaflet chordae appeared to be located in a more lateral and less useful position functionally than the basilar chordae subtending the anterior leaflet. Also, with loss of large amounts of the anterior leaflet, retaining a full posterior leaflet of the tricuspid valve became essential to provide the necessary surface area of leaflet tissue to cover the valve orifice area.

In 1988, Yee and Ullyot [5] reported on tricuspid valve repair for endocarditis in 12 patients, 4 of whom similarly required major leaflet debridement and extensive reconstructive valvoplasty. Results were very encouraging in a difficult patient population. In 3 of the 4 patients with valve reconstructions, conversion to a bicuspid valve was accomplished, similar to the technique used in our first patient. In their series, a pericardial bridge between the two leaflets was introduced. Of their 4 patients, 1 with an extensive anterior leaflet resection also required a Carpentier-Edwards ring to achieve valve competence. The current series expands on this experience and adds other options for reparative operations.

The major drawback to the method presently employed at this institution is the persistence of tricuspid valve regurgitation. Tricuspid valve repair, however, still provides a lesser degree of regurgitation than tricuspid valve excision.

As measured echocardiographically, regurgitation was reduced and right ventricular dilatation reversed in half of the patients after repair. However, as a permanent solution to tricuspid valve regurgitation as well as endocarditis, only 1 of 4 patients was left with a reasonably competent valve. According to Yee and Ullyot [5], most patients with acute tricuspid regurgitation, right ventricular volume overload, and annular distention preoperatively may be expected to have increasing competence of the tricuspid valve postoperatively with recovery of right ventricular function and decreasing annular dimensions. It was notable, however, that all 5 patients with tricuspid repair procedures reported by Dreyfus and co-workers [10] required a Carpentier ring annuloplasty to achieve valve competence, even without loss of leaflet tissue.

Compensation for extensive excision of one half to three quarters of the anterior leaflet of the tricuspid valve is a considerably different situation from excision of redundant leaflet tissue in mitral valve repair procedures. After debridement, the infected valves have major deficiencies in the total amount of leaflet tissue available for reconstruction. Resection of infected chordae and papillary muscle heads leaves little support for remaining leaflets or added pericardial patches. Many of these repair methods for endocarditis may still result in residual tricuspid regurgitation.

In the current series, every attempt was made to reconstruct the valve with existing tissue rather than add pericardium, which would be nonviable tissue, or Gore-Tex suture for chordae, which would be foreign material. Although annular plication was necessary to allow reapproximation of leaflets, all patients had annular dilatation preoperatively and so plication only helped restore normal orifice dimensions. None had tricuspid stenosis on postoperative examination.

An alternative to creation of a bicuspid leaflet with a less extensive resection might be mobilization of the remaining anterior and/or posterior leaflet base along the annular rim as a "leaflet sliding plasty" [10] until coaptation to form a new commissure could be achieved. In patient 4, late regurgitation might have been related to pericardial patch shrinkage. As flail segments were not noted on follow-up echocardiography, mobilized chordae were believed to be intact. Glutaraldehyde tanning of the pericardial patch might reduce the likelihood of late pericardial shrinkage.

The single patient in whom a Carpentier-Edwards annuloplasty ring was implanted after extensive anterior leaflet resection was left with a quite competent valve. An annuloplasty ring was not added in the other three operations for fear of introducing foreign material to the repair. However, the right ventricular enlargement and annular dilatation present in all patients undoubtedly contributed to residual regurgitation postoperatively. Annular plication and DeVega-type suture annuloplasties may not restore the natural contour of the annulus. A rigid modeled ring might have achieved valve competency but would have added a risk for reinfection.

Although excised tissue in three of four valves was positive for bacteria on both Gram stain and histology, in only 1 of 4 patients was the tissue positive for bacteria on subsequent culture. This suggests that bacteria, though present, may have been killed by preceding antibiotic therapy. In no patient did recurrent endocarditis develop postoperatively after completion of antibiotic therapy.

In view of these facts, one might consider the insertion of a Carpentier-Edwards or other structured tricuspid annuloplasty ring in any patient who had undergone 1 week or more of antibiotic therapy before operation and who had negative blood cultures immediately preoperatively. This decision would need to be made on a case by case basis, but undoubtedly the addition of an annuloplasty ring would provide the advantage of improved valve competency after tricuspid valve repair for acute endocarditis.

Valve repair in endocarditis is still a relatively new application for standard repair techniques and certainly has existing limitations. However, as more experience is gained in this field, the possibilities for native valve preservation might lead to earlier surgical treatment of infectious processes before extensive and irreparable valvar and subvalvar destruction has occurred.

References

1. Chan P, Ogilby JD, Segal B. Tricuspid valve endocarditis. Am Heart J 1989;117:1140–6.
2. Chandraratna PAN, Reagan RB, Imaizumi T, Langevin E, Elkins RC. Infective endocarditis cured by resection of a tricuspid valve vegetation. Ann Int Med 1978;89:517–8.
3. Pruett TL, Rotstein OD, Anderson RW, Simmons RL. Tricuspid valve *Candida* endocarditis: successful treatment with valve-sparing debridement and antifungal chemotherapy in a multiorgan transplant recipient. Am J Med 1986;80:116–8.
4. Jagger JD, McCaughan BC, Pawsey CGK. Tricuspid valve endocarditis cured by excision of a single vegetation. Am Heart J 1986;112:626–7.
5. Yee ES, Ullyot DJ. Reparative approach for right-sided endocarditis. Operative considerations and results of valvuloplasty. J Thorac Cardiovasc Surg 1988;96:133–40.
6. Arbulu A, Asfaw I. Tricuspid valvulectomy without prosthetic replacement: ten years of clinical experience. J Thorac Cardiovasc Surg 1981;82:684–91.
7. Robin E, Thoms NW, Arbulu A, Ganguly SN, Magnisalis K. Hemodynamic consequences of total removal of the tricuspid valve without prosthetic replacement. Am J Cardiol 1975;35: 481–6.
8. Stern HS, Sisto DA, Strom JA, Soeiro R, Jones SR, Frater RWM. Immediate tricuspid valve replacement for endocarditis. Indications and results. J Thorac Cardiovasc Surg 1986; 91:163–7.
9. Carpentier A. Cardiac valve surgery—"the French correction." J Thorac Cardiovasc Surg 1983;86:323–37.
10. Dreyfus G, Serraf A, Jebara VA, et al. Valve repair in acute endocarditis. Ann Thorac Surg 1990;49:706–13.

Intraoperative Pleural Lavage Cytology in Lung Cancer Patients

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Cytology of intraoperative pleural lavage was examined in 164 lung cancer patients who underwent pulmonary resections. None of the patients had any pleural effusion or dissemination. Cytology was performed three times: (1) at thoracotomy, (2) immediately after resection, and (3) after washing the pleural cavity with 5,000 mL of physiological saline solution just before closure of the chest wall. Twenty-three patients (14%) had more than one positive cytological finding. The frequency of positive cytological findings was significantly correlated with pathological T classification, pleural status, and pathological stage. The positive lavage group had a significantly higher recurrence rate than the negative lavage group in patients with stage I or stage II cancer. Four patients in the positive lavage group (17.4%) had recurrence in pleura or pericardium whereas only 1 patient in the negative lavage group (0.7%) had a recurrence in pericardium. The positive cytological finding of pleural lavage has more important meaning as a prognostic factor in stage I and stage II and indicates a greater possibility of recurrence in pleura or pericardium, but further examinations to evaluate the viability of detected malignant cells are required so that the positive cytological findings of pleural lavage can be regarded as subclinical pleural dissemination.

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Spjut and associates [1] reported the cytological findings of pleural cavity washings in lung cancer patients and referred to the possibility of implantation of malignant cells by incisional biopsy. Eagan and associates [2] studied the cytological findings from pleural lavage after curative pulmonary resection in 135 lung cancer patients and reported the correlation of positive cytological findings with cell type, lymph node status, visceral pleural status, and pathological stage. Kondo and associates [3] reported that the positive cytological findings were significantly correlated with pleural status and lymphatic permeation but not with histology, stage, or lymph node involvement in pleural lavage just after thoracotomy. Buhr and associates [4] reported the results of pleural lavage cytology before and after pulmonary resections and the poor prognosis of patients with positive cytological findings, and insisted that positive cytological findings of pleural lavage should be added to the criteria for the staging system. Results from previous reports differ, and the importance of pleural lavage cytology as a prognostic factor or an indicator of subclinical pleural dissemination in lung cancer patients has not been understood completely. In this report, we also present the results of cytological findings obtained from pleural lavage fluid and try to clarify the relationship of positive cytological findings with several pathological factors and results of preoperative transthoracic needle biopsy. The other aim of this study is to refer to the possibility of pleural lavage cytology to confirm subclinical pleural dissemination and its utility as a prognostic factor.

Material and Methods

The study group consists of 164 lung cancer patients who had intraoperative pleural lavage cytology examined in our institute between September 1985 and December 1988. None of the study group had any pleural effusion or pleural dissemination. All patients of the study group had three intraoperative pleural lavages: at thoracotomy, immediately after lobectomy or pneumonectomy with extensive sampling of mediastinal lymph nodes, and after routine washing of the pleural cavity with 5,000 mL of physiological saline solution just before closure of the chest wall. At each lavage, the pleural cavity was filled with 500 mL of physiological saline solution and all the saline solution was aspirated into a glass bottle with heparin. About 400 mL of the supernatant of the lavage fluid was discarded after several hours' settlement. The rest of the saline solution, including the precipitates, was shaken and centrifuged at 1,500 rpm for 5 minutes. The sedimented material was stained by the Papanicolaou method.

One hundred ninety-eight patients with lung cancer underwent pulmonary resection during the period of this study in our institute, but 34 patients were excluded from the study group: 1 had apparent pleural dissemination at thoracotomy, 14 had pleural effusion at thoracotomy, and 19 lacked more than one lavage cytology specimen.

Class 1 and class 2 were regarded as the negative cytological finding, class 4 and class 5 as the positive cytological finding. The patients whose three lavage spec-

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Table 1. Patients With Positive Cytological Findings

Patient No.	Cytology 1	Cytology 2	Cytology 3	Histology	TNM	P	Stage	Follow-up (mo)	Site of Recurrence
1	–	+	–	Sq	T1 N0 M0	P0	I	35, NED	None
2	+	+	–	Sq	T2 N0 M0	P0	I	27, DAD	None
3	–	+	±	Sq	T2 N1 M0	P0	II	8, DT	Pericardium
4	+	–	–	Sq	T3 N0 M0	P3	IIIa	23, DT	Bone
5	–	+	–	Sq	T3 N1 M0	P3	IIIa	39, DT	Lung
6	±	+	+	Sq	T4 N2 M0	P3	IIIb	24, DT	Mediastinum
7	+	–	–	Sq	T2 N3 M0	P0	IIIb	17, DT	Lung
8	+	–	–	Ad	T2 N0 M0	P2	I	22, DT	Brain, lung
9	+	–	–	Ad	T1 N0 M0	P0	I	32, NED	None
10	+	–	–	Ad	T2 N0 M0	P1	I	25, NED	None
11	+	–	–	Ad	T2 N0 M0	P2	I	30, alive	Lung
12	–	+	±	Ad	T1 N0 M0	P1	I	30, CEA elevation	. . .
13	+	–	+	Ad	T2 N0 M0	P0	I	35, NED	None
14	+	–	–	Ad	T2 N0 M0	P2	I	7, DT	Pleura
15	+	+	+	Ad	T2 N0 M0	P2	I	14, DT	Pleura
16	+	–	–	Ad	T2 N2 M0	P0	IIIa	25, NED	None
17	+	–	–	Ad	T2 N2 M0	P0	IIIa	31, alive	Lung, bone
18	–	+	+	Ad	T2 N2 M0	P2	IIIa	13, DT	SCLN
19	–	+	–	Ad	T2 N2 M0	P2	IIIa	10, DT	Liver
20	+	–	+	Ad	T3 N2 M0	P3	IIIa	14, DT	Brain, lung
21	–	+	–	Ad	T3 N2 M0	P3	IIIa	18, DT	Lung
22	–	+	+	Ad	T3 N3 M0	P3	IIIb	13, DT	Pericardium
23	–	+	–	La	T3 N0 M0	P3	IIIa	17, NED	None

Ad = adenocarcinoma; CEA = carcinoembryonic antigen; DAD = died of another disease; DT = died of tumor; La = large cell carcinoma; NED = no evidence of disease; P = pleural status; SCLN = supraclavicular lymph node; Sq = squamous cell carcinoma.

imens were all negative were defined as the negative lavage group, and the patients who had more than one specimen with a positive cytological finding were defined as the positive lavage group. Differences in histology, pathological TNM classification, pathological stage, pleural status, and presence or absence of diagnostic preoperative transthoracic needle aspiration biopsy were examined between these two groups. TNM classification and stages were determined according to the Staging System of the Union Internationale Contre le Cancer [5]. The general rules for clinical and pathological staging of lung cancer by the Japanese Lung Cancer Society [6] were adopted to divide pN1 into two subgroups: pN1a, which has involvement in the intralobar lymph nodes, and pN1b, which has involvement in the hilar lymph nodes, and also to classify pleural status into four groups as follows: P0, visceral pleura is not invaded by tumor; P1, tumor has reached but not invaded through the visceral

Table 2. Patients With Cytological Findings of Class 3

Patient No.	Cytology 1	Cytology 2	Cytology 3	Histology	TNM	P	Stage	Follow-up (mo)	Site of Recurrence
1	±	–	–	Sq	T2 N0 M0	P1	I	27, DT	Lung
2	–	±	±	Sq	T2 N0 M0	P1	I	28, DT	Bone
3	±	–	–	Sq	T2 N2 M0	P1	IIIa	12, DT	Lung
4	±	–	–	Ad	T2 N0 M0	P0	I	15, NED	None
5	–	–	±	Ad	T2 N2 M0	P0	IIIa	25, NED	None
6	±	–	–	La	T1 N1 M0	P1	II	4, DAD	None

Ad = adenocarcinoma; DAD = died of another disease; DT = died of tumor; La = large cell carcinoma; NED = no evidence of disease; P = pleural status; Sq = squamous cell carcinoma.

Table 3. Histology and Pleural Lavage Cytology

Cytology	Ad	Sq	La	Sm	Ca	Total
Negative	63	61	7	2	2	135
Positive	15 (19.2%)	7 (10.3%)	1 (12.5%)	0	0	23
Total	78	68	8	2	2	158

Ad = adenocarcinoma; Ca = carcinoid; La = large cell carcinoma; Sm = small cell carcinoma; Sq = squamous cell carcinoma.

pleura; P2, tumor has invaded the visceral pleura but not involved the parietal pleura; and P3, tumor has invaded the parietal pleura and chest wall. All patients of the study group had an exact diagnosis preoperatively by transbronchial or transthoracic biopsy, so none of them underwent diagnostic intraoperative tumor biopsy. The last follow-up was done in April 1990, and sites of recurrence were confirmed in all patients with recurrence except 1 whose site has not been found yet despite rapid elevation in the level of carcinoembryonic antigen. The χ^2 test was used for check for statistical significance and the method of Kaplan-Meier was used to calculate survival rates. The statistical significance of differences between the survival curves was examined by the generalized Wilcoxon test.

Results

The positive lavage group consisted of 23 patients, 14% of the study group. Patients of the positive lavage group are listed in Table 1. The negative lavage group consisted of 135 patients. There were 6 patients whose worst cytological findings were class 3. These 6 patients are listed in Table 2, but they were not included in either the positive or the negative lavage group.

Histology

Frequencies of positive cytological findings on pleural lavage in patients with adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are presented in Table 3. Positive cytological findings were most common in adenocarcinoma, but there was no significant difference between cell types.

Pathological T Classification

Patients with more advanced T classification had a higher frequency of positive cytological findings. There was a significant relationship between cytological findings and T classification (Table 4).

Pathological N Classification

Frequencies of positive cytological findings in each N classification are presented in Table 5. No significant differences were seen except between pN1 and pN3. Thirteen of 103 patients (12.6%) with pN0 or pN1a whose nodal involvement did not extend to the hilar lymph nodes had positive cytological findings, and 10 of 55 patients (18.2%) with pN1b, pN2, or pN3 whose nodal involvement extended to hilar or mediastinal lymph nodes had positive cytological findings, but there was no significant difference.

Pleural Status

Frequencies of positive cytological findings in patients with P0 and P1 were almost the same value, that with P2 was the second highest, and that with P3 was the highest. There was a significant relationship between frequency of positive cytological findings and pleural status (Table 6).

Pathological Stage

Frequencies of positive cytological findings in stage I, stage II, stage IIIa, and stage IIIb were 12.7%, 3.7%, 20.5%, and 42.9%, respectively. Positive cytological findings were significantly more frequent in patients with stage IIIa, stage IIIb, or stage IV (23.1%) than in those with stage I or stage II (10.4%) (Table 7).

Preoperative Transthoracic Needle Aspiration Biopsy

Preoperative transthoracic needle aspiration biopsy was performed in 39 patients. Positive cytological findings were obtained in 8 patients with it (20.5%) and in 15 patients without it (12.6%). Presence or absence of preoperative transthoracic needle aspiration biopsy had no significant relationship with the frequency of positive cytological findings.

Prognosis

The survival rates for 1 year, 2 years, and 3 years were 88.9%, 78.3%, and 69.2% in the negative lavage group

Table 4. T Classification and Pleural Lavage Cytology[a]

Cytology	T1	T2	T3	T4	Total
Negative	51	75	8	1	135
Positive	3 (5.6%)	13 (14.8%)	6 (42.9%)	1 (50.0%)	23
Total	54	88	14	2	158

[a] T1 versus T3: $\chi^2 = 13.471$, $p < 0.005$; T1 versus T4: $\chi^2 = 5.744$, $p < 0.01$; T2 versus T3: $\chi^2 = 6.285$, $p < 0.01$; T1 + T2 versus T3 + T4: $\chi^2 = 12.198$, $p < 0.005$.

Table 5. N Classification and Pleural Lavage Cytology[a]

Cytology	N0	N1	N2	N3	Total
Negative	74	29 (N1a, 16; N1b, 13)	29	3	135
Positive	12 (14.0%)	2 (6.5%) (N1a, 1; N1b, 1)	7 (19.4%)	2 (40.0%)	23
Total	86	31	36	5	158

[a] N1 versus N3: $\chi^2 = 4.906$, $p < 0.05$; N0 + N1a versus N1b + N2 + N3: $\chi^2 = 0.891$, not significant.

Table 6. Pleural Status and Pleural Lavage Cytology[a]

Cytology	P0	P1	P2	P3	Total
Negative	86	25	15	9	135
Positive	8 (8.5%)	2 (7.4%)	6 (28.6%)	7 (43.8%)	23
Total	94	27	21	16	158

[a] P0 versus P2: $\chi^2 = 6.461$, $p < 0.025$; P0 versus P3: $\chi^2 = 14.417$, $p < 0.005$; P1 versus P3: $\chi^2 = 8.018$, $p < 0.005$; P0 + P1 versus P2 + P3: $\chi^2 = 16.449$, $p < 0.005$.

and 87.0%, 50.2%, and 38.8% in the positive lavage group, respectively. The survival rate for the negative lavage group was significantly better than that of the positive lavage group (Fig 1). Forty-seven patients in the negative lavage group (34.8%) have had recurrence. On the other hand, 16 patients in the positive lavage group (69.6%) have had recurrence. The recurrence rate for the positive lavage group is significantly higher than that for the negative lavage group, but the fact that the proportion of higher stages is greater in the positive lavage group than in the negative lavage group should not be neglected; therefore, differences in recurrence rate between the two groups must be discussed in each stage. In stage I, stage II, and stage IIIa, the recurrence rate was higher in the positive lavage group; in stage IIIb they were the same (Table 8). In patients with stage I or stage II disease, the recurrence rate for the positive lavage group (54.5%) was significantly higher than that for the negative lavage group (20%). In patients with stage IIIa, stage IIIb, or stage IV disease, there was no significant difference between the results of lavage cytology and the recurrence rate (Table 9).

Sites of recurrence were classified as carcinomatous pleuritis, carcinomatous pericarditis, mediastinal or cervical lymph nodes, and distant metastases including lungs. There were 2 patients with carcinomatous pleuritis and 2 patients with carcinomatous pericarditis in the positive lavage group, though there was no patient with carcinomatous pleuritis and only 1 patient with carcinomatous pericarditis in the negative lavage group (Table 10).

Of 6 patients whose worst cytologic findings were class 3, there were 3 patients (50%) who had recurrence. Their sites of recurrence, however, were not pleura or pericardium.

Comment

We obtained the cytological findings from pleural lavage fluid at three times intraoperatively. Thirteen patients had positive cytological findings in the first lavage, 12 patients in the second lavage, and 6 patients in the third lavage. As the number of patients with positive cytological findings in each lavage is small, we considered it less meaningful to discuss the results of each pleural lavage cytology; therefore, patients who had at least one positive cytological finding were grouped together into the positive lavage group.

Twenty-three of 164 patients in the study group (14.0%) had positive cytological findings, the incidence of which had a significant relationship with pathological T classification, pleural status, and pathological stage. There was no significant relationship of positive cytological findings with lymph node involvement or histology in this study group. Previous investigators did not comment on the effect of preoperative transthoracic needle aspiration biopsy. Its presence or absence has no significant relation-

Table 7. Pathological Stage and Pleural Lavage Cytology[a]

Cytology	Stage I	Stage II	Stage IIIa	Stage IIIb	Stage IV	Total
Negative	69	26	35	4	1	135
Positive	10 (12.7%)	1 (3.7%)	9 (20.5%)	3 (42.9%)	0	23
Total	79	27	44	7	1	158

[a] Stage I versus stage IIIb: $\chi^2 = 4.570$, $p < 0.05$; stage II versus stage IIIa: $\chi^2 = 3.880$, $p < 0.05$; stage II versus stage IIIb: $\chi^2 = 8.209$, $p < 0.005$; stage I + stage II versus stage IIIa + stage IIIb + stage IV: $\chi^2 = 4.764$, $p < 0.05$.

Table 8. Recurrence Rate and Pleural Lavage Cytology in Each Stage[a]

Cytology	Stage I	Stage II	Stage IIIa	Stage IIIb	Stage IV	Total
Negative	10/69 (14.5%)	9/26 (34.6%)	23/35 (65.7%)	4/4 (100%)	1/1 (100%)	47/135 (34.8%)
Positive	5/10 (50.0%)	1/1 (100%)	7/9 (77.8%)	3/3 (100%)		16/23 (69.6%)

[a] Negative lavage group versus positive lavage group in total cases: $\chi^2 = 7.899$, $p < 0.01$.

Table 9. Recurrence Rate and Pleural Lavage Cytology

Cytology	Recurrence	NED	Total	Recurrence Rate
Stage I + stage II				
Negative	19	76	95	19/95 (20.0%)
Positive	6	5	11	6/11 (54.5%)
Stage IIIa + stage IIIb + stage IV				
Negative	28	12	40	28/40 (70.0%)
Positive	10	2	12	10/12 (83.3%)

Recurrence versus NED in patients in stage I or stage II: $\chi^2 = 6.528$, $p < 0.05$.

NED = no evidence of disease.

ship with the frequency of positive cytological findings in this series. Results from Eagan and co-workers [2] and Kondo and associates [3] are not coincident with each other and differ from that of this series. The difference of time to obtain the lavage specimen may have an influence on the cytological findings. Buhr and associates [4] reported the significant relationship of positive cytological findings with tumor extent and stage, and no relationship with histology and lymph node involvement in two lavages, just after thoracotomy and before closure of the chest wall, which is almost coincident with the results of this series. Though they did not discuss the pleural status, it is supposed to be an important factor in the positive finding of pleural lavage cytology according to the results of Eagan and co-workers [2], Kondo and associates [3], and this series.

The other purpose of this study is to clarify whether intraoperative pleural lavage cytology is useful as a prognostic factor and whether it can reveal subclinical dissemination. Moreover, it would be desirable to connect the results of pleural lavage cytology with treatment. In this series, the survival rate of the positive lavage group was significantly less than that of the negative lavage group. Furthermore, the positive lavage group had a significantly greater recurrence rate than the negative lavage group in stage I or stage II, though no significant difference between the two groups was detected in the recurrence rate in stage IIIa, stage IIIb, or stage IV. Results of pleural

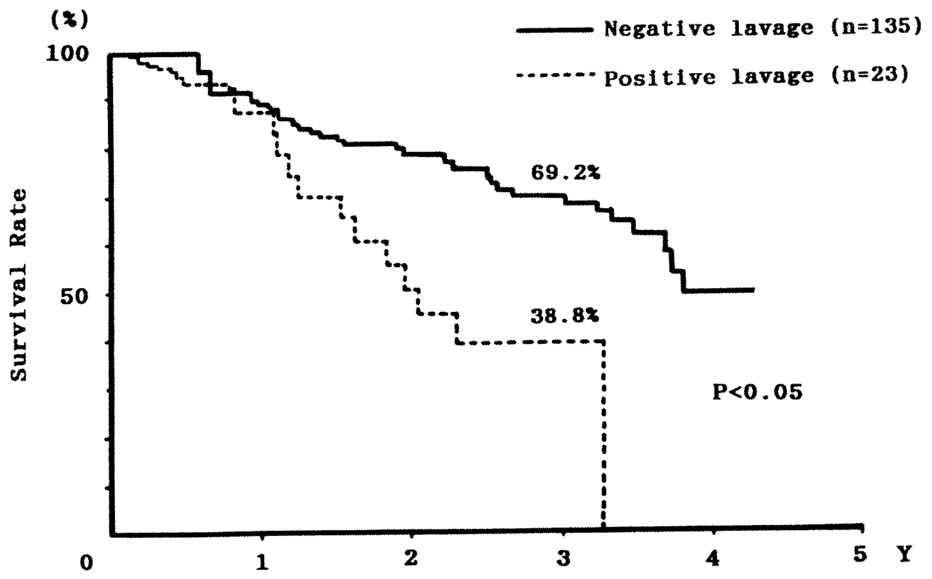

Fig 1. Survival curves for the positive lavage group and the negative lavage group.

Table 10. Sites of Recurrence and Pleural Lavage Cytology

	Cytology	
Site of Recurrence	Negative	Positive[a]
Carcinomatous pleuritis	0	2
Carcinomatous pericarditis	1	2
Mediastinal or cervical lymph nodes	9	2
Distant metastasis	34	9
Mediastinal or cervical lymph nodes + distant metastasis	3	0
Total	47	15

[a] One patient in the positive lavage group has rapid carcinoembryonic antigen level elevation, and the site of recurrence is under investigation.

lavage cytology may have greater importance as a prognostic factor in patients with stage I or stage II disease than in those with stage IIIa, stage IIIb, or stage IV disease.

As for sites of recurrence, in the negative lavage group, no patient had recurrence in the ipsilateral pleural cavity and only 1 patient had recurrence in the pericardium (0.7%, 1 of 135 patients). In contrast, in the positive lavage group there were 2 patients who had recurrence in the ipsilateral pleural cavity (8.7%, 2 of 23 patients) and 2 patients who had recurrence in the pericardium (8.7%, 2 of 23 patients). These 2 patients in the positive lavage group who had recurrence in the ipsilateral pleural cavity had pathological stage I disease. They are suspected to have occult pleural dissemination. On the other hand, 7 patients in the positive lavage group (30.4%) have no recurrence now (17 to 35 months after operation; average, 28 months), so a positive cytological finding of pleural lavage does not necessarily predict recurrence.

There are some speculations that detected malignant cells have little viability to grow in the pleural cavity or that the number of malignant cells is small enough to be removed by routine washing of the pleural cavity with 5,000 mL of physiological saline solution before closure of the chest wall. There has not been any discussion about the viability or the quantitative evaluation of detected malignant cells in pleural lavage not only in previous reports but also in this series. Further examination of these aspects is necessary. Therefore, from our point of view, a positive cytological finding of pleural lavage cannot be considered equivalent to macroscopic dissemination, so it should not be regarded as T4 in the TNM classification unless the viability of detected malignant cells is confirmed. The positive cytological finding of pleural lavage, however, means a greater possibility of recurrence in the ipsilateral pleural cavity or pericardium than a negative finding. Local instillation of chemotherapeutic agents or other kinds of local treatment should be performed postoperatively in patients with positive cytological findings of pleural lavage, especially in stage I or stage II.

References

1. Spjut HJ, Hendrix VJ, Ramirez GA, Roper CL. Carcinoma cells in pleural cavity washings. Cancer 1958;11:1222–5.
2. Eagan RT, Bernatz PE, Payne WS, et al. Pleural lavage after pulmonary resection for bronchogenic cacinoma. J Thorac Cardiovasc Surg 1984;88:1000–3.
3. Kondo H, Naruke T, Tsuchiya R, et al. Pleural lavage cytology immediately after thoracotomy as a prognostic factor for patients with lung cancer. Jpn J Cancer Res 1989;80:233–7.
4. Buhr J, Berghäuser KH, Morr H, Dobroschke J, Ebner HJ. Tumor cells in intraoperative pleural lavage. An indicator for the poor prognosis of bronchogenic carcinoma. Cancer 1990; 65:1801–4.
5. Mountain CF. A new international staging system for lung cancer. Chest 1986;89:225s–33s.
6. The Japanese Lung Cancer Society. General rules for clinical and pathological record of lung cancer. 3rd ed. Tokyo: Kanehara Shuppan, 1987:71–85.

Pleuroperitoneal Shunting for Intractable Pleural Effusions

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Pleuroperitoneal shunts were implanted in 17 patients with intractable pleural effusions, 15 of which were malignant and 2 benign. Complicating factors included 13 instances of severe trapped lung and 3 cases of synchronous ascites. There was one hospital death. Palliation of dyspnea at rest was achieved in all patients, although 3 required oxygen with exertion. Four shunts became occluded between 1 and 10 months after placement. Two of these were replaced. The remaining conduits continued to function to the present or until the patients' deaths between 1 and 28 months. Shunting allowed hospital discharge and provided symptomatic relief in a group of patients in whom other approaches had failed or were not applicable.

(Ann Thorac Surg 1991;51:605–9)

A substantial proportion of thoracic surgical practice deals with the treatment of pleural effusions that have not responded or are unlikely to respond to thoracentesis alone or treatment of the underlying condition. Although some of the pleural effusions treated by surgeons are of benign etiology, the majority are secondary to malignant disease. With the exception of a few tumors for which there is effective systemic therapy, the prognosis for these patients is grim. The goal of treatment is palliation of the patients' limiting dyspnea to allow discharge from the hospital. The method should be simple and safe, cause little discomfort, avoid prolonged hospitalization, and provide reliable relief of symptoms for at least a few months.

In most cases these goals are achieved by tube thoracostomy drainage followed by intrapleural instillation of chemical or mechanical irritants. Although usually successful, this technique fails to control the problem in 15% to 20% of cases of uncomplicated effusions. There is a higher failure rate in patients with concomitant ascites and in those with trapped lung syndrome due to fibrosis or tumor. Following the favorable report by Little and associates [1] we began using pleuroperitoneal shunts for the treatment of intractable effusions. This report describes our experience.

Material and Methods

The Shunt

The Denver pleuroperitoneal shunt (Codman and Shurtleff, Inc, Randolph, MA) is a single-unit silicone rubber conduit consisting of a unidirectional valved pumping chamber located between fenestrated pleural and peritoneal catheters. Manual compression of the shunt is required because pleural pressure is lower than peritoneal pressure. Each compression transports about 1.5 mL of fluid. The presence and location of an occlusion can be determined easily. If the chamber fails to reexpand after compression, the occlusion is at the proximal (pleural) end. If the chamber is firm and cannot be flattened by applying pressure, the blockage is on the distal (peritoneal) side (Fig 1).

Shunt placement is straightforward. A small incision is made over the sixth intercostal space at the anterior axillary line. A guidewire is passed into the pleural space using a Seldinger technique and directed posteriorly. A contiguous subcutaneous pocket is created over the anterolateral costal margin to accept the pumping chamber and provide a stable base for shunt compression. An upper quadrant muscle-splitting incision provides access for placement of two concentric pursestring sutures in the peritoneum. The two incisions are joined by a subcutaneous tunnel. The pleural limb is passed into the chest through a 16F peel-away introducer, and the pumping chamber is compressed to fill the tubing and ensure good flow. The distal catheter is passed through the pursestrings and directed toward the pelvis. The location of the pumping chamber is marked externally for postoperative use. In patients with ascites a peritoneovenous shunt is placed through the contralateral upper quadrant and tunneled to the jugular vein. We prefer to leave most of the effusion in place to maximize flow through the chamber in the early postoperative period and thereby provide the patient, family, and nurses the opportunity to become familiar with the "feel" of a normally functioning device. In the hospital the shunt is compressed approximately 25 times every 4 hours and at home for about 5 minutes three or four times a day. Adjustments to these schedules are made based on the radiographic and clinical picture. We believe it is advantageous for the pleural limb to be surrounded by fluid all of the time, thereby lessening the

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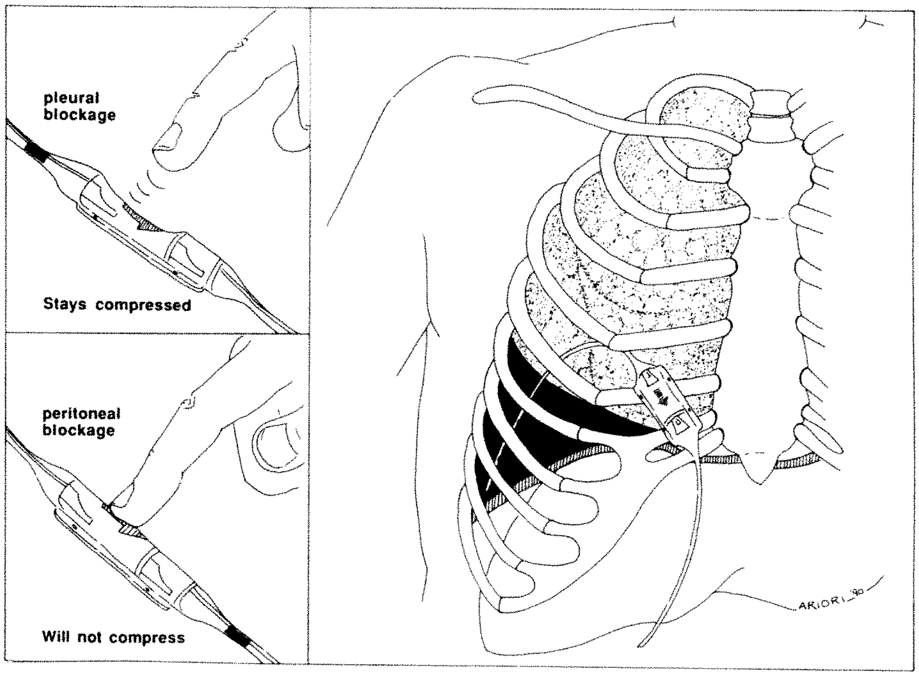

Fig 1. Diagram showing shunt position and signs of proximal or distal obstruction.

chance for tissue encroachment and occlusion. The patients are advised to cease compressions when they feel air bubbles passing though the pumping chamber, an indication that all or most of the fluid has been drained.

Patient Population

Pleuroperitoneal shunts were implanted in 17 patients, 13 women and 4 men, ranging in age from 38 to 82 years. Ten shunts drained right-sided effusions, and seven were implanted on the left. Fifteen implantations were performed with local and two with general anesthesia. Three patients had concomitant ascites and underwent simultaneous peritoneovenous shunting. Another patient required shunting later after ascites developed at 3 months. The majority of the effusions were malignant. The specific cause was lung cancer in 7 patients, breast cancer in 6, and thyroid and endometrial carcinoma in 1 each. Two patients had benign effusions, 1 with amyloidosis and 1 with pleural effusion and ascites occurring many years after treatment for lymphoma and remaining undiagnosed after multiple fluid cytological examinations and thoracoscopy.

Prior treatment of the pleural effusions consisted of tube thoracostomy in all patients. Twelve underwent unsuccessful attempts at chemical pleurodesis, 5 of them twice. In the remaining patients sclerotherapy was not tried because of extensive trapped lung. Treatment of the underlying disease included previous irradiation of the involved hemithorax in 5 patients and ongoing chemotherapy in 8 patients. Thirteen patients had radiographically apparent trapped lung syndrome and 3 had serious ascites. Only 1 of the 17 patients failed other treatment without an obvious complicating factor. During the same time period we treated 358 cases of pleural effusion by tube drainage and sclerosis. Shunting, therefore, was performed in only 4% of the entire group.

Results

One patient died 5 days after shunt placement. The clinical picture suggested sepsis from pneumonia. There was no evidence of pleural infection by thoracentesis or of abdominal sepsis by examination. The patient refused all therapeutic interventions including intravenous fluids and antibiotics. A second patient suffered a cerebrovascular accident on the fourth postoperative day due to the syndrome of thrombocytopenia and thrombosis from prophylactic low-dose heparin and was discharged only after a long hospitalization. No other early problems were encountered. The remaining patients were discharged within 1 week except in cases of ongoing inpatient cancer treatment. All patients experienced substantial alleviation of their dyspnea at rest. Thirteen had no limitation with moderate exertion. Three patients with serious underlying lymphangitic parenchymal tumor involvement, however, remained limited with varying degrees of exertion required during the activities of daily living. Home oxygen therapy was required in these 3 patients. With the exception of the stroke patient shunt compressions were performed without difficulty by the patients and their families. There was no clinical evidence of peritoneal seeding caused by the transport of malignant cells into the abdomen. In fact, the single patient in whom ascites developed 3 months after shunt placement had primary systemic amyloidosis rather than carcinoma as the cause for his pleural effusion.

Nine of the 16 shunts in discharged patients remained patent until the patients' deaths between 1 and 28 months after placement (mean, 8 months). Three patients remain alive with functioning conduits at 2, 3, and 5 months after placement. There were four instances of shunt occlusion, occurring at 1, 6, 7, and 10 months after implantation. Three of these shunts became occluded at the pleural end

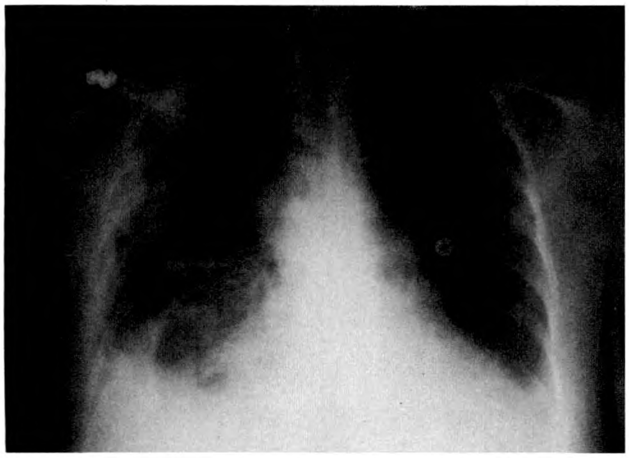

Fig 2. (Patient 1.) Chest radiograph after fluid drainage shows trapped lung and a thick cortex of tumor.

by tumor growth and fragmentation in patients with breast cancer and massive pleural involvement. The fourth shunt became blocked by thrombus in the pumping chamber in a patient with lung cancer treated with anticoagulation for pulmonary emboli. Two of the 4 patients with occluded shunts were considered terminal and did not undergo shunt revision. The other two occluded devices were replaced. One functioned well until the patient's death from disseminated tumor 2 months later, and the other remains patent 5 months after replacement. There were no occlusions in the cases of combined pleuroperitoneal and peritoneovenous shunts.

Illustrative Cases

Patient 1

A 35-year-old woman with breast carcinoma had dyspnea and a large right pleural effusion. Cytological examination confirmed the presence of malignant cells. Tube thoracostomy yielded more than 3 L of fluid and resulted in dramatic relief of her dyspnea. The chest radiograph after drainage showed massive pleural tumor and failure of the lung to reexpand (Fig 2). Two instillations of tetracycline were carried out, but the chest tube output remained high and serial films showed no improvement in lung expansion. Within 2 days of tube removal the hemithorax had filled with fluid, and the patient was again bedridden because of dyspnea. Repeated thoracenteses produced substantial but transient improvement. In an effort to provide palliation a pleuroperitoneal shunt was placed and produced marked alleviation of symptoms. Although the radiograph in the early period after implantation continued to demonstrate trapped lung, the patient no longer required oxygen and was discharged home with minimal limitation of activity. A chest radiograph 4 months later showed a surprising degree of lung reexpansion (Fig 3). She was seen 6 months later with bilateral pleural effusions, pericardial effusion, and ascites, with all four areas shown to communicate by methylene blue injection. Shunt removal showed occlusion by blood and tumor fragments. Replacement along with peritoneovenous shunting and pericardial drainage provided minimal palliation. Spinal cord compression developed from tumor invasion, and the patient died after a long hospital stay.

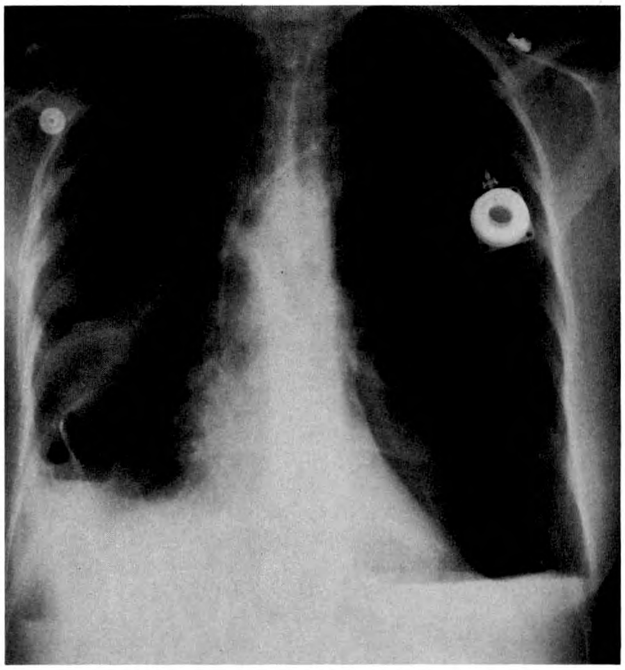

Fig 3. (Patient 1.) Chest radiograph 4 months after shunt insertion shows considerable lung reexpansion. A venous access port is now in place because clinical improvement after shunting allowed resumption of chemotherapy.

This case demonstrates several important points. First, the patient was an excellent candidate for a shunt because her symptoms were entirely related to pleural effusion and there was clear documentation of improvement each time fluid was drained. Six months of excellent palliation were achieved in an otherwise hopeless situation. Second, tumor fragmentation and bleeding are common causes of shunt blockage and generally signify progression of local disease that precludes successful palliation by shunt replacement. The patient's advanced metastases at her second admission also made replacement unwise. Third, clinical improvement is often dramatic despite radiographic findings of continued failure of lung reexpansion. We believe this is the result of relief of tension in the hemithorax with a decrease in the work of breathing.

Patient 2

A recurrent right pleural effusion developed in a 69-year-old woman with adenocarcinoma of the lung 3 months after thoracoscopy, tube thoracostomy, and sclerotherapy. Considerable lymphangitic parenchymal involvement was apparent radiographically after fluid removal (Fig 4). Because drainage produced moderate amelioration of her shortness of breath, a shunt was placed. Subsequently she no longer required oxygen at rest but

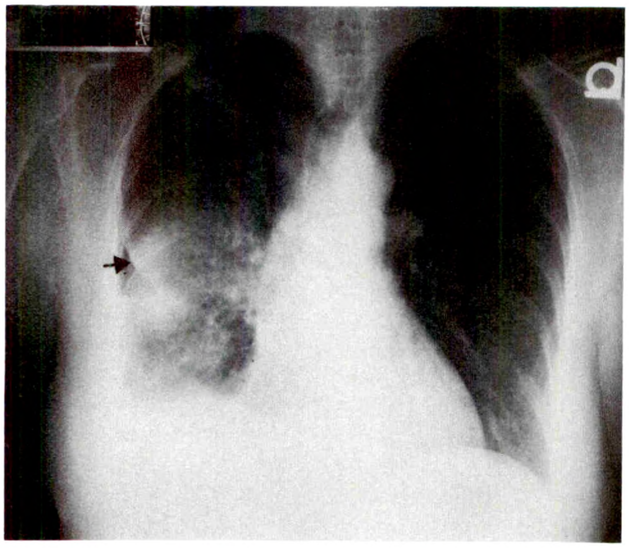

Fig 4. (Patient 2.) Chest radiograph showing both trapped lung (arrows) and lymphangitic tumor involvement.

continued to require supplementation on exertion. Shunting permitted her to be discharged and remain at home until her death 2 months later.

When the patient's pulmonary symptoms are caused by more than the pleural effusion, it is imperative to document that treatment of the effusion alone will provide satisfactory palliation before recommending shunt insertion. Parenchymal tumor involvement as well as intrinsic or external bronchial obstruction are frequently associated with malignant effusions and may be the primary cause of the patient's difficulty. Those who remain dyspneic at rest after drainage and have no hope of a comfortable existence are not candidates for shunting. Often, as in this case, the decision is difficult. The patient's subjective assessment is the major factor, although oxygen saturation or blood gases at rest and with exertion may be helpful.

Patient 3

Dyspnea from a large right pleural effusion developed in a 38-year-old woman with advanced breast carcinoma. Tube drainage produced relief of symptoms, but sclerosis failed due to trapped lung. A pleuroperitoneal shunt provided good palliation for 7 months, when debilitating dyspnea recurred and examination showed proximal limb occlusion. A computed tomographic scan demonstrated tumor growth around the catheter (Fig 5). Accordingly, shunt replacement was not advised. The patient was treated with supportive measures only and died during this admission.

As noted previously, shunt occlusion is often caused by tumor fragmentation or growth causing obliteration of most of the pleural space. Patients with bulky intrapleural disease are especially at risk for this problem. Shunt revision is futile if there is no longer a substantial space to drain. Computed tomographic scanning is an excellent means of defining the amount of tumor mass and the location, size, and geometry of any residual fluid collections. In contrast to this case, the computed tomographic scan of another patient whose shunt became occluded demonstrated a large homogeneous fluid collection and absence of tumor progression (Fig 6). A hemothorax had developed in him 6 months after anticoagulation for pulmonary emboli was begun. He continues to do well 7 months after replacement of the clotted shunt, irrigation of the hemithorax, and cessation of anticoagulation.

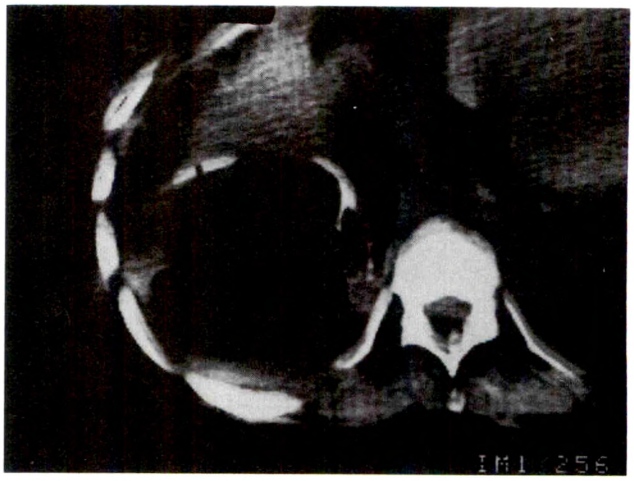

Fig 5. (Patient 3.) Computed tomographic scan performed after proximal shunt occlusion showing tumor growth around the catheter and absence of a large collection amenable to drainage.

Patient 4

A 48-year-old woman with metastatic breast carcinoma was seen with severe limitation due to large bilateral pleural effusions and ascites. Sclerotherapy failed because of continuing high output on both sides and trapped lung on the right. Combined right pleuroperitoneal and peri-

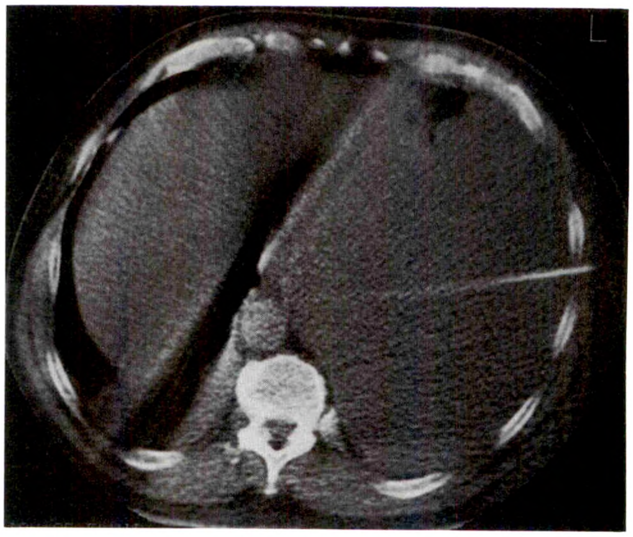

Fig 6. Computed tomographic scan performed after shunt occlusion showing a large homogeneous collection surrounding the pleural catheter. In this situation shunt replacement was beneficial.

toneovenous shunts were placed. The left-sided drainage decreased thereafter and a second instillation of tetracycline was successful. The patient was discharged and achieved satisfactory palliation until her death at home 2 months later.

The simultaneous occurrence of ascites and bilateral effusions is not uncommon, especially in patients with gynecological malignancies. Treatment is difficult and generally requires control of fluid in all three cavities, because the ascites may communicate with the pleural spaces and prevent chemical pleurodesis. Although further experience in this difficult setting is required, this case suggests that combined shunting might allow enough "drying out" of the nonshunted pleural space to permit pleurodesis.

Comment

The mean survival of patients with malignant pleural effusion is only 3 months, with 1-month and 6-month mortality rates of 54% and 85% [2]. Treatment options after unsuccessful tube drainage and sclerotherapy are limited and generally unsatisfactory. Prolonged tube drainage or repeated thoracenteses have been used in these patients but are associated with risks of infection, hemorrhage, protein depletion, and further loculation of an already complex pleural space. In addition, the necessity for ongoing hospitalization or frequent physician visits limits the palliative benefit of these approaches. Operative decortication of the involved lung can be quite effective but is associated with substantial morbidity and mortality [3], and is, we believe, applicable to only a small minority of patients. Because of their short life expectancy, their often debilitated status, and the lack of a simple yet effective means of treatment, we have previously not been able to provide acceptable palliation for our patients with intractable malignant pleural effusions. In contrast, our results with pleuroperitoneal shunting in these difficult cases has been gratifying.

The reported experience with pleuroperitoneal shunting has also been favorable [4–9]. Little and colleagues have described the largest series [10]. Good to excellent palliation was achieved in 83% of their 29 patients. Little and colleagues came to consider the pleuroperitoneal shunt an alternative to traditional tube drainage and sclerotherapy because of its effectiveness, comfort, and short hospital stay. In contrast to our patients, therefore, a minority of their cases had trapped lung (7) or had undergone prior attempted chemical pleurodesis (8).

The recent series reported by Tsang and associates [11] is similar to ours in that shunting was reserved as secondary therapy in complex situations. All 16 of their patients had trapped lung syndrome. One patient died in the early postoperative period. Good palliation was achieved in 14 of the remaining 15 patients. Two shunts became occluded, one by infected debris and one by thrombus. All other shunts remained functional at the time of the report or until the patients' deaths between 1.5 and 23 months after implantation. There was one instance of possible peritoneal tumor seeding 23 months after shunt placement.

Pleuroperitoneal shunting should be considered in patients with symptomatic pleural effusions when conventional treatment has failed or is considered likely to fail. The procedure is safe and simple and can usually be carried out with local anesthesia and sedation. Most patients are capable of caring for their shunts after a few days of training. Early hospital discharge and a comfortable period at home without the need for frequent medical visits can be achieved in properly selected cases. Relief of dyspnea at rest is the rule. Exertional dyspnea, activity level, and the need for home oxygen availability are determined mainly by the status of the underlying lung parenchyma. Shunt function can be determined simply by physical examination. The mechanical effects of tumor progression most often account for early occlusion and generally preclude successful revision. Computed tomographic scanning can identify the few patients in whom replacement might be beneficial. Most conduits, however, remain patent for the duration of the patients' lifespans.

Contraindications to shunting include inability to compress the pump, pleural infection, multiple loculations, an obliterated peritoneal space, severe limitations unrelated to the pleural effusion, and, most importantly, failure of fluid drainage to provide symptomatic improvement sufficient to allow a reasonable outpatient existence. The last two considerations often require considerable clinical judgment in this group of very ill patients.

References

1. Little AG, Ferguson MK, Golomb HM, Hoffman PC, Vogelzang NJ, Skinner DB. Pleuroperitoneal shunting for malignant pleural effusions. Cancer 1986;58:2740–3.
2. Chernow B, Sahn SA. Carcinomatous involvement of the pleura. Am J Med 1977;63:695–702.
3. Martini N, Bains MS, Beattie EJ. Indications for pleurectomy in malignant pleural effusion. Cancer 1975;35:734–8.
4. Weese JL, Schouten JT. Pleural peritoneal shunts for the treatment of malignant pleural effusions. Surg Gynecol Obstet 1982;154:391–2.
5. Husain SA. Pleuroperitoneal shunt in recurrent pleural effusions. Ann Thorac Surg 1986;41:609–11.
6. Cimochowski GE, Joyner LR, Fardin R, Sarama R, Maran A. Pleuroperitoneal shunting for recalcitrant pleural effusions. J Thorac Cardiovasc Surg 1986;92:866–70.
7. Murphy MC, Newman BM, Rodgers BM. Pleuroperitoneal shunts in the management of persistent chylothorax. Ann Thorac Surg 1989;48:195–200.
8. Pope AR, Joseph JH. Pleuroperitoneal shunt for pneumonectomy cavity malignant effusion. Chest 1989;96:686–8.
9. Brofman JD, Hall JB, Scott W, Little AG. Yellow nails, lymphedema and pleural effusion: treatment of chronic pleural effusion with pleuroperitoneal shunting. Chest 1990;97:743–5.
10. Little AG, Kadowaki MH, Ferguson MK, Staszek VM, Skinner DB. Pleuro-peritoneal shunting: alternative therapy for pleural effusions. Ann Surg 1988;208:443–50.
11. Tsang V, Fernando HC, Goldstraw P. Pleuroperitoneal shunt for recurrent malignant pleural effusions. Thorax 1990;45:369–72.

Cardiorespiratory Responses to Hypertonic Saline Solution in Cardiac Operations

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Infusion of small volumes of hypertonic saline solution (HS) seems to be of benefit in patients with impaired perfusion. The cardiorespiratory response to a 7.2% NaCl solution prepared in hydroxyethylstarch (HES) solution was investigated prospectively in patients undergoing prolonged cardiopulmonary bypass (CPB) (HS-HES group; n = 15); 6% HES 200/0.5 solution was infused in a control group (HES group; n = 15). Volume was given preoperatively to double low pulmonary artery occlusion pressure (<4 mm Hg) within 20 minutes. Hemodynamics, oxygen transport variables, and pulmonary gas exchange were studied before and after infusion as well as before and after CPB. Significantly less HS-HES solution (3.06 ± 0.2 mL/kg) than 6% HES 200/0.5 solution (10.3 ± 0.9 mL/kg) was necessary to double baseline pulmonary artery occlusion pressure. Fluid balance during CPB was negative in the HS-HES patients (−0.05 mL/kg · min CPB) and was lowest in this group even 5 hours after CPB. Mean arterial pressure, pulmonary arterial pressure, and heart rate were without differences between the groups. Changes in cardiac index (+40%) and total systemic resistance (−25%) were significantly most pronounced in the HS-HES patients, continuing even until the end of operation. Pulmonary gas exchange (arterial oxygen tension, intrapulmonary right-to-left shunting) was least compromised in these patients, particularly after bypass. Oxygen consumption was without difference between the groups; oxygen delivery increased significantly more in the HS-HES patients due to the larger increase in cardiac output. It can be concluded that preoperative infusion of the new HS-HES solution was of advantage for our patients: hemodynamics were improved significantly, fluid requirement during CPB was reduced, and pulmonary gas exchange was less compromised after CPB in these patients. Thus, hypertonic solutions might offer a valuable aspect for volume replacement in cardiac surgery patients.

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The increased sensibility to the risks associated with the transfusion of homologous blood [1] has forced clinicians to use nonsanguineous volume replacement more aggressively. A sufficient increase in circulating volume is the primary goal in the treatment of volume deficits. However, the ideal mode of fluid restoration should provide adequate improvement in macrocirculation *and* microcirculation while minimally affecting oxygen transport variables and fluid balance [2–4].

In addition to crystalloids and colloids hypertonic solutions are gaining more interest as a "new" fluid replacement regimen [5–9]. They appear to improve cardiovascular function on multiple levels [10–12]: (1) displacement of tissue fluid into the blood compartment; (2) direct vasodilatory effects, in both the systemic and pulmonary circulation; (3) reduction in venous capacitance; and (4) positive inotropic effects through direct actions on the myocardial cells. Infusion of mere hypertonic saline solution was reported to possess only transient volume stabilizing effects [13]; the expansion of the plasma volume by an osmotic fluid shift is a short effect, because only a small amount of fluid is really added, and once the salt has been equilibrated no more additional fluid is retained. To prevent this water leakage was the motivation for preparing hypertonic NaCl solution in colloids, ie, in dextran, by which an increase in blood volume could be sustained [6, 14].

The purpose of this study was to evaluate efficacy of and cardiorespiratory responses to administration of a hypertonic saline solution prepared in hydroxyethylstarch solution (HS-HES solution) in coronary artery patients undergoing longer lasting cardiopulmonary bypass procedures and to compare it with a "standard" 6% HES 200/0.5 solution.

Material and Methods

Patients and Grouping

A total of 30 patients undergoing elective aortocoronary bypass grafting were studied after informed consent was obtained from each patient according to the protocol of the Human Ethics Committee of the hospital. Excluding criteria were a severely reduced myocardial function (left ventricular ejection fraction < 0.40; left ventricular end-diastolic pressure > 30 mm Hg), renal malfunction (creatinine level > 130 μmol/L [1.5 mg/dL]), and β-blocking therapy. All patients had a pulmonary artery occlusion

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pressure (PAOP) of less than 4 mm Hg after induction of anesthesia and the period of cardiopulmonary bypass (CPB) was expected to be greater than 100 minutes (more than five-vessel disease).

The patients were randomly divided into 2 groups receiving either a new 7.2% hypertonic saline solution prepared in HES solution (osmolarity 2,400 mosm/L; 60 g/L 6% HES 200/0.5 [Fresenius, Bad Homburg, Germany]) (HS-HES group; n = 15) or a "standard" HES solution (6%; mean molecular weight 200.000; degree of substitution 0.5 [Fresenius]) (HES group; n = 15) to double reduced baseline PAOP value within 20 minutes before onset of the operation.

Anesthesia and Cardiopulmonary Bypass

Introduction and maintenance of anesthesia were performed in a standardized manner using weight-related doses of fentanyl (total dose, 33.1 ± 3.0 μg/kg), midazolam (total dose, 0.61 ± 0.1 mg/kg), and pancuronium bromide (total dose, 0.25 ± 0.01 mg/kg); with regard to anesthesia no statistical differences could be demonstrated between the groups. All patients were on controlled mechanical ventilation within the investigation period (inspired oxygen fraction, 1.0; zero end-expiratory pressure). In the intensive care unit, inspired oxygen fraction was adjusted according to blood gas analyses; for better interpretation arterial oxygen tension/inspired oxygen fraction was used.

Cardiopulmonary bypass was carried out with a nonpulsatile pump and membrane oxygenators (Sorin 41; Sorin, Turino, Italy). The circuit was primed with 1,000 mL of 5% dextrose solution, 1,000 mL of Ringer's solution, 250 mL of albumin 5% and electrolytes (20 mval potassium, 50 mL sodium 10%); a flow of 2.4 L/min · m^2 was maintained during moderate hypothermia (esophageal temperature, 34.2° ± 0.5°C). One liter of Bretschneider's cardioplegic solution (based on low sodium [15 mmol/L] and absence of calcium, contains mannitol [20 mmol/L] and is buffered with histidine [180 mmol/L], intracellular type of cardioplegic solution) was given initially for myocardial protection. A two-stage cannula was used for venous return into the circuit, and the operation was performed in "partial bypass" (monoatrial-cannulation technique). During bypass the lungs were kept statically inflated with a positive end-expiratory pressure of 5 cm H_2O. Within 20 minutes after start of CPB, blood from the extracorporeal circuit was concentrated using an ultrafiltration device (hemofilter HF-80; Fresenius) to remove as much ultrafiltrate as used cardioplegic solution. When necessary, Ringer's solution was added to the heart-lung machine to maintain filling volume. During weaning off bypass as much pump blood as necessary to keep PAOP greater than 7 mm Hg but less than 13 mm Hg was infused. After termination of CPB, the residual blood of the extracorporeal oxygenation equipment was concentrated using the HF-80 system, and the autologous blood was retransfused until the end of the operation.

Volume infusion (Ringer's solution when PAOP was less than 7 mm Hg; packed red cells when the hemoglobin value was less than 90 g/L) as well as administration of catecholamines during and after weaning off bypass were given as indicated by anesthesiologists not involved in the study.

Data Points and Measured Variables

Heart rate, mean arterial pressure, pulmonary arterial pressure, PAOP, cardiac output (thermodilution technique), and right atrial pressure were recorded, and derived variables (cardiac index, total systemic resistance) were calculated as well. Blood gas analyses were carried out from arterial as well as mixed-venous blood samples; oxygen consumption, oxygen delivery, and intrapulmonary right-to-left shunting were calculated by standard formulas [3]. Sodium concentration and blood osmolarity were measured from arterial blood samples. Measurement of hemodynamics was performed and blood samples were taken:

0. After induction of anesthesia (in hemodynamic steady state, before volume infusion = baseline values)
1. After doubling PAOP by volume application
2. 40 minutes after completing volume infusion
3. After termination of bypass (10 minutes after CPB, after decanulation)
4. At the end of the operation (45 minutes after termination of CPB)
5. 5 hours after termination of CPB (in intensive care unit).

Fluid balances (volume input, urine output, blood loss) during CPB and in the intensive care unit were also calculated.

Statistics

All variables are expressed as mean values and standard deviation. One-factor and two-factor analyses of variance followed by Scheffé's test were used for statistical interpretation. Values of *p* less than 0.05 were considered significant.

Results

Demographic data as well as data from CPB were without differences between the two groups (Table 1). Significantly less hypertonic solution (3.06 ± 0.2 mL/kg) than standard HES solution (10.3 ± 0.9 mL/kg) was necessary to double the baseline PAOP value. Fluid balance during CPB was negative in the HS-HES patients (−0.08 mL/kg · min CPB), whereas HES patients had a positive fluid balance (+0.14 mL/kg · min CPB). Fluid balance was even lower in the HS-HES group during the first 5 hours after CPB (see Table 1). In the intensive care unit, less Ringer's solution was used in the HS-HES patients than in the HES patients (see Table 1). The amount of ultrafiltrate removed during and after bypass was without differences between the groups. Autologous blood prepared by the HF system from the pump blood after termination of CPB was comparable for both groups (HS-HES, 870 ± 100 mL; HES, 890 ± 130 mL). None of the patients received homologous blood or blood products before, during, or after bypass (including the first 5 hours).

Table 1. Demographic, Fluid Balance, and Cardiopulmonary Bypass Data for the Two Groups[a]

Variable	HS-HES	HES
Age (y)	57.1 ± 6.6	60.6 ± 4.1
Weight (kg)	79.5 ± 6.0	79.3 ± 6.3
LVEF	0.71 ± 0.11	0.72 ± 0.07
LVEDP (mm Hg)	10.2 ± 4.1	11.8 ± 2.5
CPB (min)	115 ± 5.9	110 ± 6.8
Ischemia (min)	79 ± 10.1	75 ± 8.8
Fluid balance during CPB (mL/kg · min)	−0.08 ± 0.01[a]	+0.14 ± 0.02
Fluid balance 5 h after CPB (mL/kg · min)	−0.03 ± 0.01[a]	−0.01 ± 0.01
Ringer's solution 5 h after CPB (mL)	1,000 ± 200	1,200 ± 250

[a] Values shown as mean ± standard deviation. [b] $p < 0.05$ versus HES group.

CPB = cardiopulmonary bypass; HES = 6% hydroxyethylstarch 200/0.5 solution; HS-HES = hypertonic saline solution in hydroxyethylstarch solution; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction.

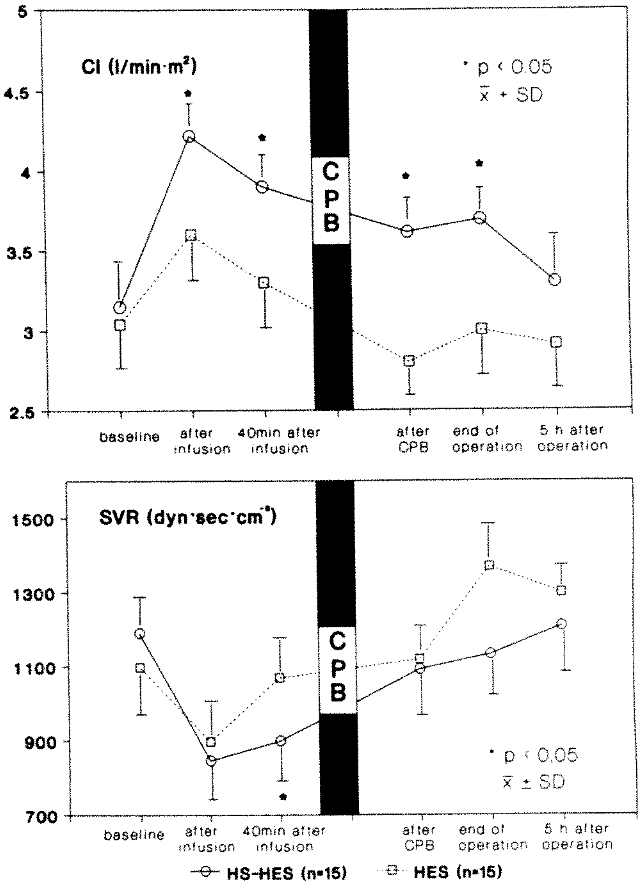

Fig 1. Changes in cardiac index (CI) and systemic vascular resistance (SVR) in the two groups.

During weaning from CPB epinephrine was necessary more often and at a higher dosage in the HES group (5 patients, 6.2 ± 1.1 μg/min) than in the HS-HES patients (2 patients, 4.0 ± 1.0 μg/min). With regard to hemodynamics no difference in mean arterial pressure, heart rate, and pulmonary arterial pressure between groups could be observed during the entire investigation period (Table 2). Cardiac index (Fig 1) increased in both groups, with a significantly greater increase in the HS-HES group (+40%). Cardiac index was greatest in these patients even after CPB. Total systemic resistance decreased significantly most in the HS-HES patients (−25%) (see Fig 1). Filling pressures (PAOP, right atrial pressure) increased after volume infusion in both groups but remained, however, significantly elevated in the HS-HES patients (Fig 2). After CPB, pulmonary gas exchange (arterial oxygen tension) was least compromised in HS-HES group and remained at the baseline level until the end of the investigation, whereas in the HES patients arterial oxygen tension decreased after bypass (Fig 3). Intrapulmonary right-to-left shunting was not changed in the HS-HES

Table 2. Hemodynamic Changes and Changes in Sodium Concentration and Osmolarity in the Two Groups[a]

Variable	Group	Baseline (0)	After Volume (1)	40 Minutes After Volume (2)	After CPB (3)	End of Operation (4)	5 Hours After Operation (5)
MAP (mm Hg)	HS-HES	81.0 ± 9.2	81.5 ± 8.2	85.3 ± 11.1	91.8 ± 8.7	97.3 ± 7.4	88.3 ± 8.0
	HES	80.5 ± 11.1	85.3 ± 5.1	80.0 ± 10.1	81.2 ± 10.1	100.1 ± 5.9	80.1 ± 6.9
HR (min^{-1})	HS-HES	74.1 ± 10.2	73.1 ± 12.1	80.5 ± 8.8	96.3 ± 12.1	95.3 ± 11.9	90.3 ± 7.7
	HES	72.3 ± 10.4	71.7 ± 10.1	85.8 ± 9.9	95.6 ± 10.1	95.2 ± 9.1	94.2 ± 9.6
PAP (mm Hg)	HS-HES	16.5 ± 2.0	20.8 ± 4.4	20.7 ± 5.4	20.7 ± 4.8	19.0 ± 2.5	20.1 ± 3.3
	HES	15.5 ± 1.9	19.3 ± 2.5	19.7 ± 4.0	18.9 ± 3.0	19.2 ± 2.8	19.0 ± 4.0
Na^+ (mmol/L)	HS-HES	143 ± 3.5	150 ± 1.9[b]	149 ± 2.2[b]	144 ± 4.0	146 ± 3.0	144 ± 4.2
	HES	141 ± 2.3	141 ± 4.0	142 ± 3.6	139 ± 4.1	143 ± 4.0	142 ± 3.9
Osmolarity (mosm/L)	HS-HES	308 ± 3.9	316 ± 6.8[b]	317 ± 2.0[b]	318 ± 3.6	314 ± 4.5	310 ± 4.0
	HES	307 ± 4.1	307 ± 4.8	309 ± 3.3	312 ± 5.0	314 ± 4.6	309 ± 3.1

[a] Values shown as mean ± standard deviation. [b] $p < 0.05$ versus HES group.

HES = 6% hydroxyethylstarch 200/0.5 solution; HR = heart rate; HS-HES = hypertonic saline solution in hydroxyethylstarch solution; MAP = mean arterial pressure; PAP = pulmonary arterial pressure.

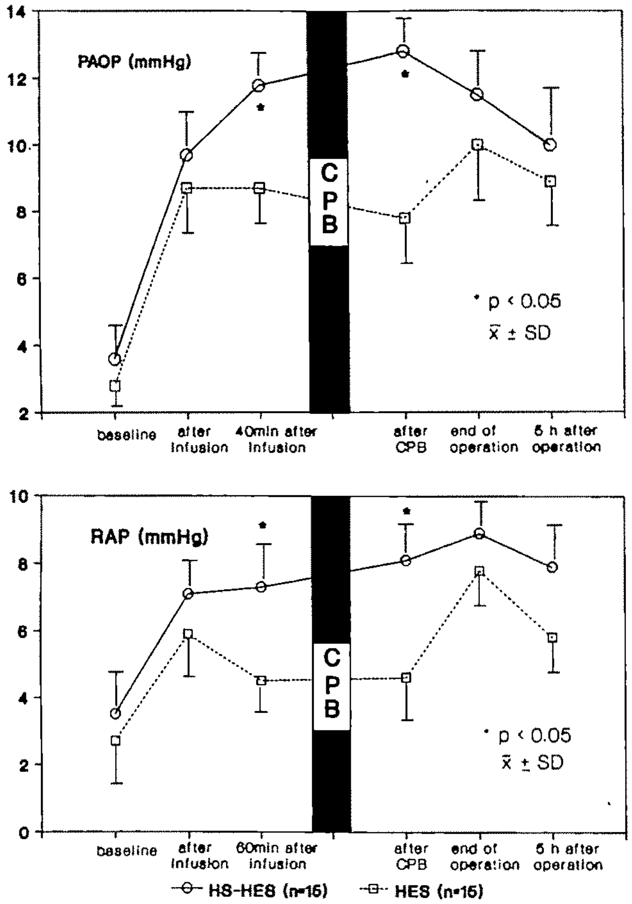

Fig 2. Changes in pulmonary artery occlusion pressure (PAOP) and right atrial pressure (RAP) in the two groups.

group, but was increased in the HES patients after termination of bypass (see Fig 3). Oxygen consumption was without difference between the groups; oxygen delivery, however, increased significantly in the HS-HES patients. The increase in oxygen delivery remained even after weaning off bypass (Fig 4). Sodium concentration increased after infusion of the HS-HES solution but never exceeded 153 mmol/L (see Table 2), and it returned to values less than 145 mmol/L by the first postoperative day. Osmolarity also increased in the HS-HES patients, without exceeding 320 mosmol/L (see Table 2). After CPB, there were no more differences between the groups with regard to sodium concentration and osmolarity.

None of the patients suffered from sequelae attributable to the study. Routinely monitored cerebral function was without differences between the groups. All patients were discharged from the intensive care unit at the third postoperative day at the latest and showed no differences in their postoperative course.

Comment

The use of hypertonic infusion for treatment of hypovolemia is not new: in 1919 Penfield [15] used hyperosmolar crystalloid injections in severe hemorrhagic shock. Several experimental and clinical data support the superiority of relatively small volumes of hypertonic saline solution in improving hemodynamics and outcome in comparison with much larger amounts of isotonic solution [5, 7, 16]. DeFelippe and associates [17] studied the effects of 7.5% NaCl (2,400 mosm/L) in patients with terminal refractory, hypovolemic shock: 11 of 12 patients were successfully treated by infusion of hypertonic NaCl solution. Mazzoni and co-workers [18] documented by a mathematical model that after a 20% hemorrhage the addition of hypertonic solution amounting to one-seventh of the shed blood volume. reestablished blood volume within 1 minute. This calculated effect could be verified by subsequent animal experiments.

The initial improvement in cardiovascular function represented by an increase in cardiac output seems to be mediated by the hypertonicity of the solution; the solute composition does not seem to be important. However, maintenance of these cardiovascular responses is more dependent on solute than on hypertonicity [8]. Beneficial effects of hypertonic saline solution were reported to be rather transient [13]. Thus, the hypertonic solution was mixed with a colloid, ie, dextran, which resulted in a significant prolongation of its efficacy [6, 14]. In the present study, hypertonic solution was prepared in HES solution due to its substantially less anaphylactic potency

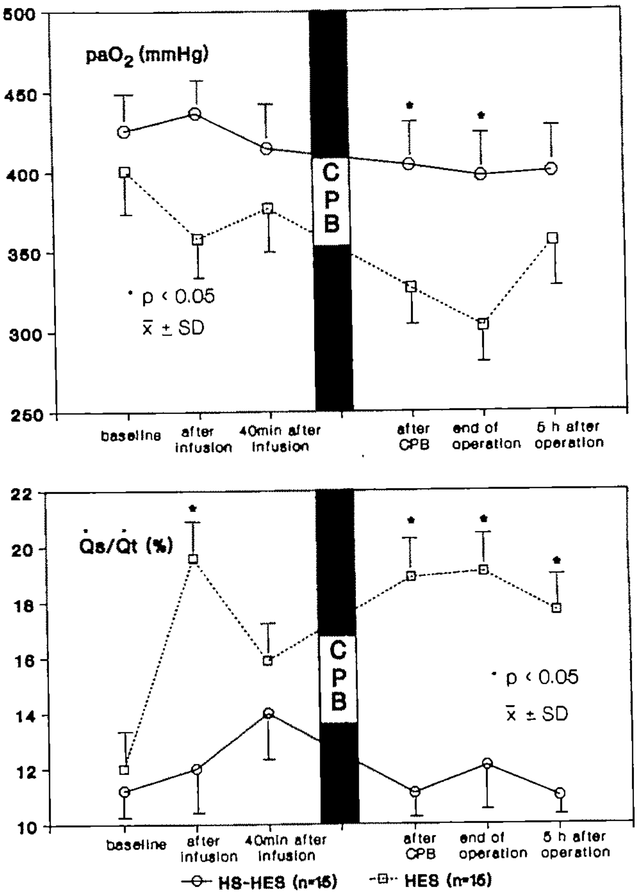

Fig 3. Changes in arterial oxygen tension (paO_2) and intrapulmonary right-to-left shunting ($\dot{Q}s/\dot{Q}t$) in the two groups.

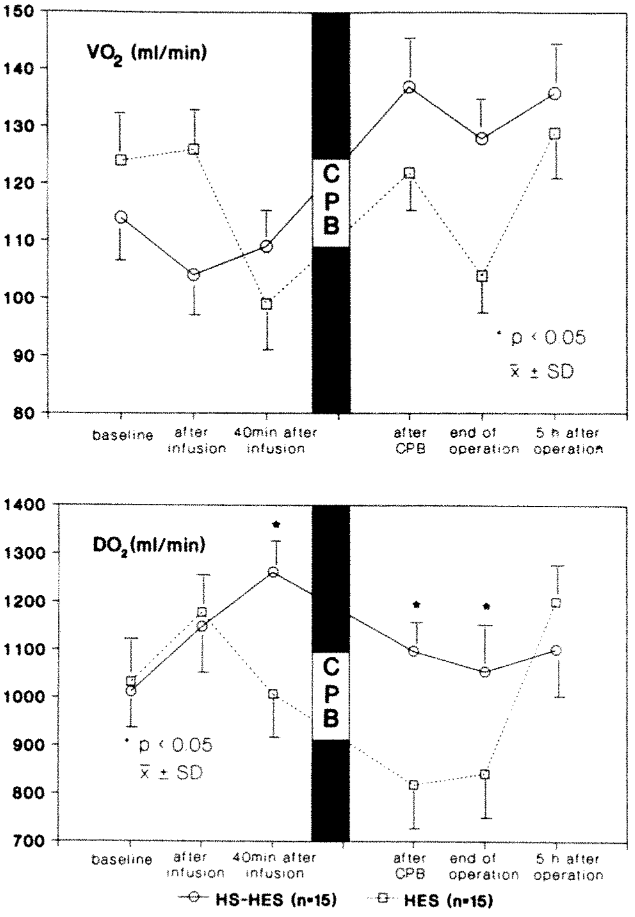

Fig 4. Changes in oxygen consumption (VO_2) and oxygen delivery (DO_2) in the two groups.

and smaller coagulation impairment compared with dextran [19]. We have chosen a "standard" HES solution as control because using it an effective restoration of hemodynamic stability as well as oxygen transport could be achieved. Thus, HES solution is widely accepted for correction of volume deficits, even in cardiac surgery [19].

Fluid administration in our study increased cardiac output promptly in both groups and decreased total systemic resistance significantly, which can be explained by a decrease in viscosity and an increased cardiac index. Both hemodynamic changes were most pronounced in the patients who received HS-HES and were not transient, but lasted until the end of CPB. Oxygen consumption was not changed by infusion of HS-HES solution, whereas oxygen delivery was increased significantly in these patients, most likely due to a more pronounced increase in cardiac output.

One of the major findings in this study was the reduction in fluid balance during CPB. This effect of the solution has to be stressed in these patients: according to Utley and Stephens [20], fluid balance during CPB summed up to 800 mL/kg · h of bypass. Breckenridge and associates [21] found a routine fluid accumulation during CPB summing up to a 33% increase in the measured extracellular fluid space postoperatively. In the present investigation fluid balance was lowest in the HS-HES patients even 5 hours after bypass.

When evaluating a new volume therapy in cardiac surgery not only hemodynamic effects are of interest; particular alterations associated with CPB have to be taken into consideration as well. Shires and colleagues [22] outlined the altered physiological function of cell membranes as a result of a low flow state: shock and trauma lead to extravasation of water and electrolytes into the interstitium. Cardiopulmonary bypass has to be regarded as an induced form of shock with an unphysiological nonpulsatile perfusion, low-pressure perfusion, and an impaired microcirculation induced by a release of various mediator systems [23].

In addition to the effective stabilization of macrohemodynamics, another potential beneficial effect of the hypertonic solution is the improvement in microhemodynamics. Besides direct vasodilatory properties, extraction of fluid from the capillary endothelium might be of importance. Mazzoni and associates [18] supposed that the hemodilution and endothelial cell shrinkage result in a decreased capillary hydraulic resistance. By this shrinkage of the endothelium the inner diameter of the capillary will be enhanced, resulting in decreased resistance. The concomitant decrease in viscosity by infusion of hypertonic solution will result in a reduction in hydraulic resistance of the capillaries. As swollen endothelium is observed after ischemia this aspect might be of particular interest in cardiac surgery patients, in whom both the lungs and the myocardium are subjected to a period of sustained ischemia during the period of CPB. Although we did not perform electronic microscopy, the improved pulmonary function after CPB (arterial oxygen tension and intrapulmonary right-to-left shunting not altered, which was in contrast to the control group) in our patients who received hypertonic HES solution before bypass might be explained not only by its fluid-reducing effects but also by an improvement in capillary tissue perfusion. This supports evidence that the lungs seem to be well protected against interstitial fluid accumulation and the negative effects associated with CPB. Moreover, it was demonstrated that application of hypertonic solution for resuscitation prevents an increase in pulmonary vascular resistance often described during the shock state and after CPB [24]. Thus, this hypertonic solution might be advantageous not only by an effective improvement in hemodynamics but also by a reduction in complications secondary to trauma such as CPB.

Alterations of the integrity of the capillary membrane seem to be dependent on duration of bypass [25]. Thus, an extensive positive fluid balance during CPB will directly alter pulmonary function thereafter [24]. Bypass times were prolonged, but still moderate (<130 minutes) in this study. However, in patients undergoing more complicated cardiac surgical procedures with long-lasting CPB (>200 minutes) these fluid-reducing effects (and postulated improvement in microhemodynamics) might be even more beneficial. It would be reasonable to assume that less fluid requirements during CPB will be correlated with less pulmonary organ impairment and other sequelae [24].

There are, however, some theoretical problems when using hypertonic saline solutions: extreme hypernatremia and hyperosmolarity may result in cerebral dysfunction such as disorientation, confusion, and even seizure by disruption of the blood-brain barrier [7]. However, the sodium concentration in none of our patients exceeded 153 mmol/L, osmolarity was always less than 330 mosm/L, and none of our patients had signs of cerebral dysfunction (by electroencephalographic monitoring during operation) or cerebral complications in the postoperative period. Moreover, serum osmolarity of 350 mosm/L without complications has been reported in humans [26]. In the present study, no differences in sodium and osmolarity between the groups were obvious after CPB. Nevertheless, when using hypertonic solutions for volume therapy, close measurements of sodium and osmolarity are of importance.

It can be concluded that infusion of hypertonic saline solution prepared in HES solution resulted in an effective, and not only transient, improvement in hemodynamics. Patients undergoing lengthy CPB procedures will profit from this fluid regimen by a less pronounced fluid requirement during bypass and an improvement in microcirculation associated with less pronounced alterations in pulmonary organ function in the period after bypass.

References

1. Miller RD, Bove JR. Acquired immune deficiency syndrome and blood products. Anesthesiology 1983;58:493–4.
2. Edwards JD, Nightingale P, Wilkins RG, Faragher EB. Hemodynamic and oxygen transport response to modified fluid gelatin in critically ill patients. Crit Care Med 1989;17:996–8.
3. Shoemaker WC, Hauser CJ. Critique of cristalloid versus colloid therapy in shock and shock lung. Crit Care Med 1979;7:117–24.
4. Shoemaker WC. Relation to oxygen transport patterns to the pathophysiology and therapy of shock states. Int Care Med 1987;13:230–4.
5. Armistead CW, Vincent JL, Preiser JC, DeBaker D, Minh TL. Hypertonic saline solution-hetastarch for fluid resuscitation in experimental septic shock. Anesth Analg 1989;69:714–20.
6. Kreimeier U, Meßmer K. New perspectives in resuscitation and prevention of multiple organ system failure. In: Baethmann A, Messmer K, eds. Surgical research: recent concepts and results. Berlin, Heidelberg: Springer, 1987:39.
7. Maningas PA, Bellamy RF. Hypertonic sodium chloride solution for the prehospital management of traumatic shock: a possible improvement in the standard of care? Ann Emerg Med 1986;15:1411–4.
8. Smith GJ, Kramer GC, Perron P, Nakayama SI, Gunther RA, Holcroft JW. A comparison of several hypertonic solutions for resuscitation of bled sheep. J Surg Res 1985;39:517–28.
9. Velasco IT, Pontieri V, Silva RE, Lopes OU. Hyperosmotic NaCl and severe hemorrhagic shock. Am J Physiol 1988;239: H664–73.
10. Read RC, Johnson JA, Vick JA. Vascular effects of hypertonic solutions. Circ Res 1960;8:538–44.
11. Baue AE, Tragus ET, Parkins WM. A comparison of isotonic and hypertonic solutions and blood on blood flow and oxygen consumption in the initial treatment of hemorrhagic shock. J Trauma 1967;7:743–56.
12. Koch-Weser J. Influence of osmolarity of perfusate on contractility of mammalian myocardium. J Physiol (Lond) 1958; 143:515–40.
13. Nakayama SI, Sibley L, Gunther RA, Holcroft JW, Kramer GC. Small-volume resuscitation with hypertonic saline (2.400 mOsm/liter) during hemorrhagic shock. Circ Shock 1984;13: 149–59.
14. Maningas PA, DeGuzman LR, Tillman FJ, Hinson CS, Priegnitz KJ, Volk KA. Small volume infusion of 7.5% NaCl/6% dextran 70 for the treatment of severe hemorrhagic shock in swine. Ann Emerg Med 1986;15:1131–7.
15. Penfield WG. The treatment of severe and progressive haemorrhage by intravenous injections. Am J Physiol 1919;48: 121–8.
16. Shackford SR, Sise MJ, Fridlund PH, et al. Hypertonic sodium lactate versus lactated Ringer's solution for intravenous fluid therapy in operations on the abdominal aorta. Surgery 1983;1:41–51.
17. DeFilippe J, Timoner J, Velasco IT, Lopes OU, Rocha E, Silva M. Treatment of refractory hypovolemic shock by 7.5% sodium chloride injections. Lancet 1980;2:1002–4.
18. Mazzoni MC, Borgström P, Arfors KE, Intaglietta M. Dynamic fluid redistribution in hyperosmotic resuscitation of hypovolemic hemorrhage. Am J Physiol 1988;255:H629–37.
19. London ML. Plasma expansion in cardiovascular surgery: practical realities, theoretical concerns. J Cardiothorac Anesth 1988;6 (Suppl 1):39–49.
20. Utley JR, Stephens DB. Fluid balance during cardiopulmonary bypass. In: Utley JR, ed. Pathophysiology and technique of cardiopulmonary bypass, vol I. Baltimore: Williams & Wilkins, 1982:23.
21. Breckenridge IM, Diggerness SB, Kirklin JW. Increased extracellular fluid after open intracardiac operation. Surg Gynecol Obstet 1970;131:53–8.
22. Shires GT, Cunningham JN, Barker CRF. Alterations in cellular membrane function after large hemorrhage. Ann Surg 1972;176:288–95.
23. Chenoweth E, Cooper SW, Hugli, Stewart RW, Blackstone EH, Kirklin JW. Complement activation during cardiopulmonary bypass. Evidence for generation of C3a and C5a anaphylatoxins. N Engl J Med 1981;304:497–503.
24. Peters RM. Effects of cardiopulmonary bypass on lung function. In: Utley JR, ed. Pathophysiology and technique of cardiopulmonary bypass, vol II. Baltimore: Williams & Wilkins, 1983:164.
25. Wisselink P, Feola M, Alfrey CP, Suzuki M, Ross JL, Kennedy JH. Prolonged partial cardiopulmonary bypass and the integrity of small blood vessels. J Thorac Cardiovasc Surg 1970;60:789–95.
26. Monafo WW, Chuntrasakul C, Ayvazian V. Hypertonic sodium solution in the treatment of burn shock. Am J Surg 1973;126:773–80.

Closed Heart Cryoablation of the His Bundle Using an Anterior Septal Approach

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His bundle cryosurgical ablation using a closed heart anterior septal approach was used in 6 patients. There were 3 men and 3 women, aged 24 to 73 years. Three patients had atrial fibrillation and 2 patients had atrial flutter (2 with combined episodes of atrial tachycardia). One patient had atrial tachycardia. Five patients had no structural heart disease and 1 patient had left ventricular dilatation (ejection fraction, 0.35). All patients undergoing His bundle cryosurgical ablation had permanent heart block without intraoperative complications (mean follow-up, 25 months). Closed heart anteroseptal cryoablation of the His bundle is effective and is an alternative to attempted catheter ablation.

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His bundle ablation is an alternative electrophysiological intervention in select patients with problematic supraventricular tachycardia [1, 2]. Catheter ablation is the current preferred intervention. Surgical ablation may be carried out after attempted catheter ablation in patients without contraindication to medial sternotomy [3–5]. We report our experience with a closed heart cryosurgical ablation of the His bundle using an anterior septal approach [6] that does not require cardiopulmonary bypass or intracardiac manipulations.

Material and Methods

Surgical Anatomy

Surgical anatomy of the atrioventricular (AV) node–His bundle region has been studied by Lev [7] and by Sealy and associates [8, 9]. The following description is based on a macroscopic dissection of the region carried out in our laboratory [10]. Briefly, the AV node–His bundle system comprises: (1) the compact AV node and His bundle encased in a dense fibrotic sheath within the inferior edge of the atrial membranous septum, (2) the penetrating node where it enters the right fibrous trigone (central fibrous body), (3) the intermediate AV node, and (4) the atrial inputs to the AV node.

The atrial membranous septum that harbors the AV node–His bundle can be epicardially approached by dissection of the right coronary fossa (anterior septal region) (Fig 1), which is the juxtaaortic segment of the right AV sulcus. The right coronary fossa resembles a toppled pyramid with three walls and a base corresponding to the epicardial surface of the abundant fat pad, which fills the fossa. The right coronary fossa is deep and expansive. The three walls of the right coronary fossa are: (1) the posterolateral wall of the right ventricular infundibulum; (2) the anteromedial wall of the right atrium, which medially unites with the medial wall of the right atrium to constitute part of the atrial septum posterior to the aortic root; and (3) the medial wall of the fossa, which is constituted by the aortic root, the aortic annulus, and the right anterior trigone. The walls of the fossa angle upward, forming an inverted pyramid. It is abundantly fat-filled, roofed by the epicardium (base of the pyramid), and overlapped by the right atrial appendage. Through the right coronary fossa runs the first segment of the right coronary artery, which courses over the posterolateral wall of the right ventricle over its infundibular segment. The atrial membranous septum is subjacent to the right anterior trigone and situated at the very summit of the inverted pyramidal space.

After dissection of the coronary fossa, a cryoprobe (5 mm in diameter) can be positioned over the atrial membranous septum and the AV node–His bundle ablated. Therefore, we elected to surgically approach the AV node through the anterior septal region.

Patient Population

The study population consisted of 6 patients aged 24 to 73 years (mean age, 53 years) with refractory supraventricular tachyarrhythmias (Table 1). Duration of symptoms varied from 1 to 60 years (mean, 15 years). All patients were severely disabled by recurrent arrhythmias despite intensive antiarrhythmic therapy (mean, 4.5 antiarrhythmic drugs per patient) and attempted cardioversions. Two patients had atrial fibrillation. Two patients had atrial flutter. In 1 patient, flutter was associated with ectopic focus atrial tachycardia. Patient 6 had recurrent atrial fibrillation and sick sinus syndrome with concealed bypass tract. Five patients had no structural heart disease with normal cardiac function. Patient 3 had insulin-dependent diabetes and coronary artery disease with a left ventricular ejection fraction of 0.35.

All patients underwent electrophysiological assessment to determine the functional properties of their AV con-

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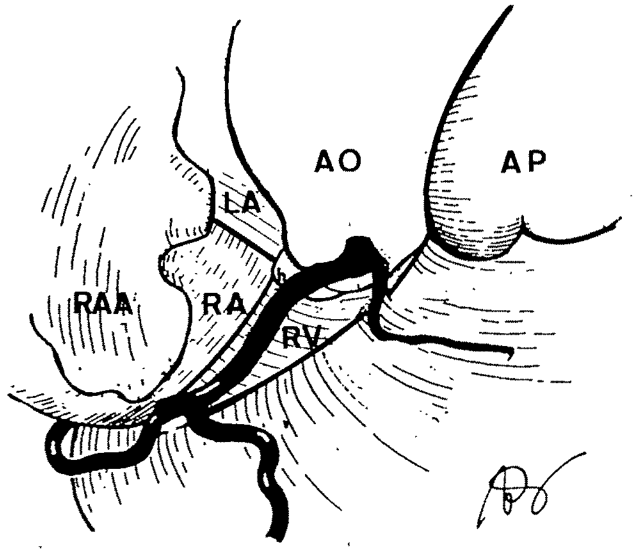

Fig 1. The right coronary fossa is abundantly fat-filled, roofed by the epicardium, and overlapped by the right atrial appendage (RAA). Through the right coronary fossa runs the first part of the right coronary artery. The three walls of the fossa are: (1) the posterolateral wall of the right ventricular infundibulum (RV); (2) the anteromedial wall of the right atrium (RA); and (3) the medial wall, constituted by the aortic root, aortic annulus, and right anterior trigone. The compact atrioventricular node–His bundle is encased in a dense fibrotic sheath within the inferior edge of the atrial membranous septum (h). (AP = pulmonary artery; LA = left atrium.)

Table 2. Preoperative Electrophysiological Data

Patient No.	PA (ms)	AH (ms)	HV (ms)	Inducible Arrhythmia	Catheter Ablation (No. of shocks)
1	50	100	45	JR	+ (10)
2	. . .	. . .	. . .	. . .	+
3	40	65	45	AFL	+ (3)
4	50	140	35	. . .	–[a]
5	40	50	30	. . .	+ (5)
6	70	40	40	AFL	–[a]

[a] Catheter ablation not attempted due to inability to record an adequate His potential.

AFL = atrial flutter; JR = junctional rhythm.

duction system and to detect accessory AV pathways (Table 2). Atrioventricular conduction was normal in all patients except in patient 4, who had prolonged AV nodal conduction time (AH interval, 140 ms). His bundle ablation was indicated because of symptomatic drug-resistant supraventricular tachycardia not amenable to direct surgical electrophysiological intervention. His bundle catheter ablation was attempted in 4 patients using radiofrequency current [11]. In 2 patients, catheter ablation was not considered because of inadequate His bundle electrical potential recordings.

Surgical Technique

The heart is exposed using a median sternotomy. A pair of temporary pacing electrodes are attached onto the right atrium and the right ventricle and connected to an external dual-chamber pacemaker.

The anterior septal region is approached in a manner similar to that used for ablation of right anterior paraseptal accessory AV pathways [12]. The right coronary fossa is exposed by deflecting the right atrial appendage superiorly and to the right, using a stay suture tied at the apex of the appendage (Fig 2). The ascending aorta is slightly deflected to the left by a broad tape passed around it. The epicardium of the fat pad is incised along its reflection onto the right atrial wall. Right cardiac veins are identified and tied. The fat pad is mobilized en bloc and the tricuspid annulus is exposed. The aortic root is dissected free and the aortic annulus is identified. The atrial membranous septum subjacent to the aortic annulus is seen as a whitish thin-walled membrane. The dissection is completed to obtain maximal exposure of the atrial membranous septum that harbors the AV node-His bundle.

The His bundle is localized using ice mapping (Fig 3): the oblique tip of a 5-mm-diameter cryoprobe is positioned over the atrial membranous septum and cooled at −5°C. The tip of the cryoprobe is on the His bundle if complete heart block occurs shortly after the onset of cooling. Several attempts may be necessary to find the best position. Cryoablation is obtained by cooling the cryoprobe to −70°C during 2 minutes and by performing

Table 1. Patient Data Summary

Patient No.	Age (y)	Sex	Arrhythmia Diagnosis	Duration of Symptoms (y)	Number of Drugs	Follow-up (mo)
1	36	M	AFL/AT	5	5	43
2	73	F	AF	60	5	41
3	67	M	AFL	2	2	20
4	62	M	AF	17	3	19
5	24	F	AT	6	6	15
6	58	F	AF/AVRT	1	6	14

AFL = atrial flutter; AF = atrial fibrillation; AT = ectopic atrial focus tachycardia; AVRT = atrioventricular reentrant tachycardia using concealed pathway.

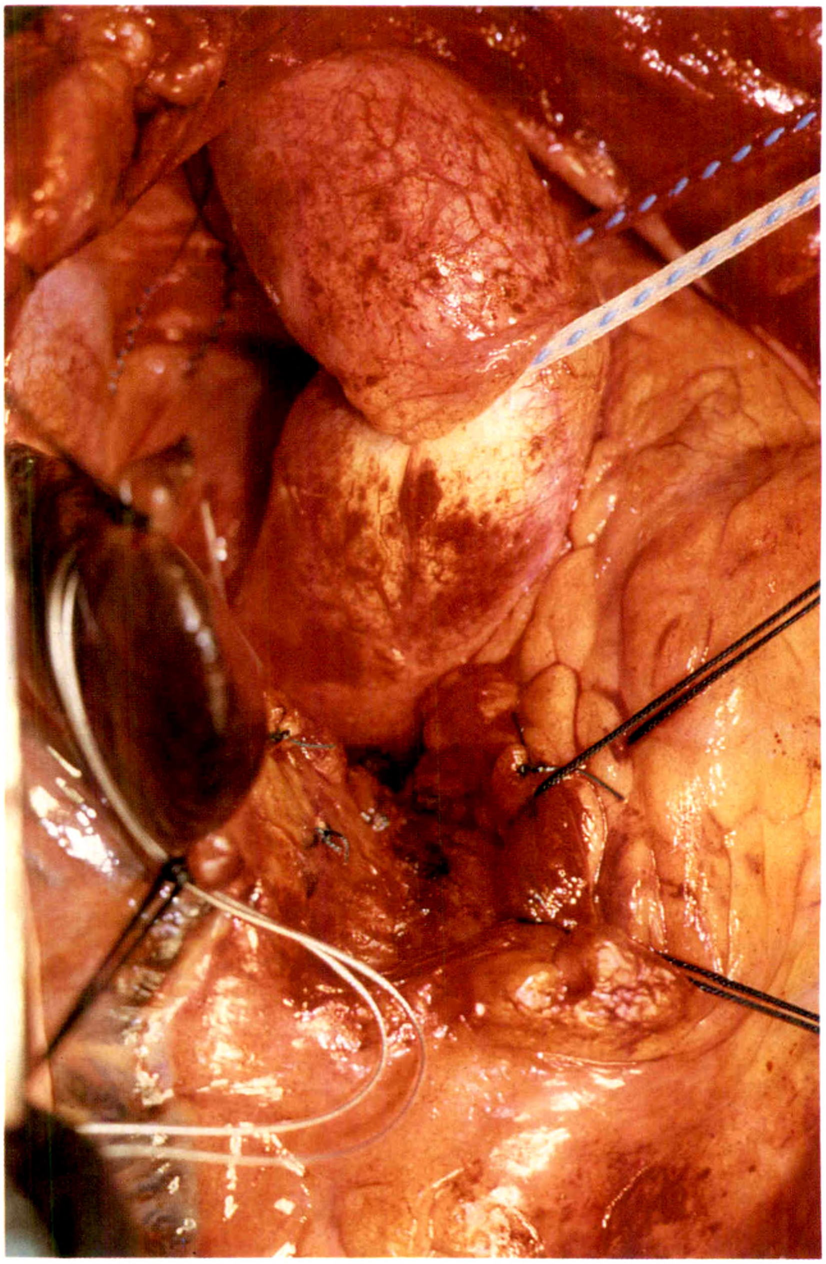

Fig 2. Operative view depicting exposure and dissection of the right coronary fossa. The atrioventricular fat pad has been mobilized and deflected toward the right ventricular wall using two sutures passed around it. The aortic root is well seen. The right atrial wall, which has been dissected, and the right atrial appendage deflected by a ligature are on the left side of the photograph. The right ventricular wall (infundibulum) is on the right side of the photograph. The summit of the pyramidal space corresponds to the atrial membranous septum. On the left side of the photograph, behind the aorta, is depicted the left atrium, where two temporary pacing wires have been attached.

several applications of the cryoprobe in the same area. Ventricular pacing is usually started after cryoablation but atrial pacing is necessary during ice mapping if the heart is in junctional or irregular atrial rhythm to determine when AV block occurs.

Epicardial leads for permanent pacing were implanted in 2 patients. In the remaining patients, cardiac pacing was established using temporary electrodes, and a permanent endocardial pacemaker was implanted 5 to 7 days postoperatively when complete heart block was assured.

Results

There were no intraoperative complications. Permanent complete heart block was obtained in all patients, and no patient required antiarrhythmic therapy postoperatively. Follow-up was completed in all patients and averaged 25 months (range, 14 to 43 months). There was no arrhythmia recurrence. One patient had pacemaker dysfunction due to a broken epicardial lead 3 months after operation. An endocardial lead was implanted and connected to the same pacemaker generator. A late sternal wound infection developed in patient 3 and necessitated removal of sternal wires followed by extensive debridement. All patients have returned to full-time activities.

Comment

Our early experience confirms that endocardial pacing leads should be used because epicardial leads are less

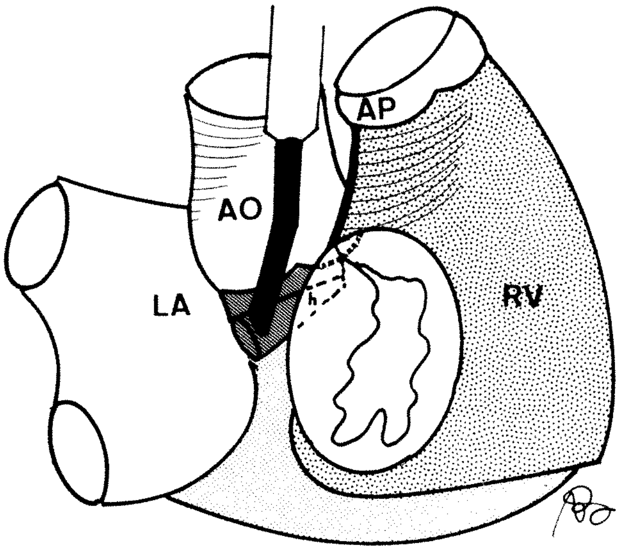

Fig 3. The His bundle is localized using ice mapping: the oblique type of a cryoprobe 5 mm in diameter is positioned over the membranous septum containing the atrioventricular node–His bundle (h) *and cooled at −5°C.* (AO = *aorta;* AP = *pulmonary artery;* LA = *left atrium;* RV = *right ventricle.)*

reliable and durable. Temporary epicardial wires allow temporary control of the heart block and implantation of an endocardial pacemaker when the permanent block is assured.

Cryosurgical ablation of the AV node–His bundle system using an endocardial approach guided by His bundle electrophysiological mapping has been well established after the original study by Harrison and associates [13], the surgical experience of Sealy and co-workers [8, 9], and the clinical long-term follow-up by Klein and colleagues [14]. Recently, Bredikis [15] described a cryosurgical ablative technique that does not require cardiopulmonary bypass but only intracardiac manipulations. The cryoprobe is introduced into the right atrium through an atrial incision encircled by a pursestring suture while the index finger is introduced in a similar manner to guide the tip of the cryoprobe. Permanent complete heart block was obtained in 29 of 34 patients by this method.

Our technique does not require cardiopulmonary bypass or intracardiac manipulation. Precise dissection and exposure of the atrial membranous septum based on well-identified anatomical landmarks was associated with uniform AV node–His bundle cryoablation and may become a more acceptable alternative after failed catheter ablation.

Other surgical alternatives are being developed for resistant atrial tachycardia, mainly for lone atrial fibrillation such as the corridor operation [16] or Maze [17] as an alternative to His bundle ablation and implantation of permanent pacing. However, their therapeutic role is not established as yet.

References

1. Scheinman MM, Morady F, Hess DS, Gonzalez R. Catheter induced ablation of the atrioventricular junction to control refractory supraventricular arrhythmias. JAMA 1982;248: 851–5.
2. Gallagher JJ, Svenson RH, Kasell JH, et al. Catheter technique for closed-chest ablation of the atrioventricular conduction system. A therapeutic alternative for the treatment of refractory supraventricular tachycardia. N Engl J Med 1982; 306:194–200.
3. Johns JA, Black AJ, Harper RW, et al. Control of refractory supraventricular arrhythmias after unsuccessful closed-heart His bundle ablation. PACE 1985;8:85–93.
4. Cole HM. Diagnostic and therapeutic technology assessment (DATTA). Ablation of accessory pathways in the Wolff-Parkinson-White syndrome. Ablation of His bundle. JAMA 1987;258:542–4.
5. Lemery R, Brugada P, Della Bella P, et al. Predictors of long-term success during closed chest catheter ablation of the atrioventricular junction. Eur Heart J 1989;10:826–32.
6. Guiraudon GM. His bundle cryosurgical ablation using a closed heart epicardial approach. J Am Coll Cardiol 1989;13: 175A.
7. Lev M. The conducting tissues. In: Gould SE, Thomas CC, eds. Pathology of the heart. 2nd ed. Springfield, IL: Charles C. Thomas, 1960:132–65.
8. Sealy WC. His bundle interruption for reentry tachycardia in Wolff-Parkinson-White syndrome. Ann Thorac Surg 1983;36: 345–51.
9. Sealy WC, Gallagher JJ, Kasell J. His bundle interruption for control of inappropriate ventricular responses to atrial arrhythmias. Ann Thorac Surg 1981;32:429–38.
10. Guiraudon GM, Klein GJ, Sharma AD, Yee R, Kaushik RR, Fujimura O. Skeletonization of the atrioventricular node for reentrant tachycardia: experience with 32 patients. Ann Thorac Surg 1990;49:565–73.
11. Landberg JJ, Chin MC, Rosenquist M, et al. Catheter ablation of the atrioventricular junction with radiofrequency energy. Circulation 1989;80:1527–35.
12. Guiraudon GM, Klein GJ, Sharma AD, Yee R, Pineda EA, McLellan DG. Surgical approach to anterior septal accessory pathways in 20 patients with the Wolff-Parkinson-White syndrome. Eur J Cardiothorac Surg 1988;2:201–6.
13. Harrison L, Gallagher JJ, Kasell J, et al. Cryosurgical ablation of the A-V node-His bundle. A new method for producing A-V block. Circulation 1977;55:463–70.
14. Klein GJ, Sealy WC, Pritchett ELC, et al. Cryosurgical ablation of the atrioventricular node-His bundle: long-term follow-up and properties of the junctional pacemaker. Circulation 1980;61:8–14.
15. Bredikis J. Cryosurgical ablation of atrioventricular junction without extracorporeal circulation. J Thorac Cardiovasc Surg 1985;90:61–7.
16. Guiraudon GM, Klein GJ, Yee R, Leitch JW, Kaushik RR, McLellan DG. Surgery for atrial tachycardia. PACE 1990;13: 1996–9.
17. Cox JL, Schuessler RB, Boineau JP. Surgery for atrial fibrillation. In: Cox JL, ed. State of the art reviews. Cardiac surgery. Cardiac arrhythmia surgery. Philadelphia: Hanley & Belfus, Inc, 1990;4,1:207–17.

Oxygenated Cardioplegia: The Metabolic and Functional Effects of Glucose and Insulin

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Reports differ as to the efficacy of glucose and insulin as cardioplegic additives. Although deliberate oxygenation of crystalloid cardioplegic solutions improves myocardial protection, little is known about the protection afforded by glucose and insulin in such oxygenated solutions. In the isolated working rat heart, we studied the addition of oxygen, glucose, and insulin, separately and together, to a cardioplegic solution. The solution was equilibrated with O_2 or N_2, with glucose added as a substrate or sucrose as a nonmetabolizable osmotic control, with or without insulin. Hearts were arrested for 2 hours at 8°C by multidose infusions. Oxygenation decreased lactate production and improved high-energy phosphate and glycogen preservation during arrest, prevented ischemic contracture, and improved functional recovery. The addition of glucose to the oxygenated solution increased the level of adenosine triphosphate at end-arrest from 10.5 ± 0.5 to 13.9 ± 0.6 nmol/mg dry weight and glycogen stores from 18.7 ± 2.5 to 35.7 ± 5.5 nmol/mg dry weight. The further addition of insulin did not better preserve these metabolites. Improvements in functional recovery due to glucose or insulin in the oxygenated solution attained statistical significance when both additives were included. Glucose increased lactate production significantly only when the solution was nitrogenated. Insulin added to the nitrogenated glucose-containing solution increased adenosine triphosphate and glycogen levels after 1 hour of arrest; and, although insulin did not prevent ischemic contracture from developing during the latter part of arrest with profound depletion of these metabolites, functional recovery was improved. The mechanism of improved functional recovery by insulin is not clear. Whether aerobic or anaerobic metabolism is favored during arrest modifies the effects of glucose and insulin. The data support the use of a fully oxygenated cardioplegic solution containing glucose, and perhaps insulin, for myocardial protection, and suggest that these additives may be beneficial whether the cardioplegic solution is deliberately oxygenated or not.

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Uncertainty persists as to whether the addition of glucose and insulin to hyperkalemic cardioplegic solutions (CSs) is justified. Some studies conclude that the addition of glucose to CSs accelerates anaerobic metabolism of the arrested heart and improves myocardial protection [1, 2]. Others maintain that the addition of glucose is not helpful [3] or that glucose with or without insulin may even be detrimental in the ischemic state [4]. The cardioplegic solutions in these studies [1–4] were not deliberately oxygenated and therefore contained little oxygen [5]. Little is known about the protection afforded by glucose and insulin in crystalloid cardioplegic solutions that are fully oxygenated [6].

Our laboratory [5, 7, 8] and others [6, 9] have previously demonstrated that full oxygenation of crystalloid CSs improves protection during hypothermic arrest. We recently demonstrated that the addition of glucose to an oxygenated CS further improves functional recovery after arrest [10]. We theorized [10] that this combined effect of oxygen and glucose is due to stimulation of aerobic metabolism, increased availability of substrate, and a decrease in anaerobic metabolism and its potentially deleterious products [11]. Oxygenation substantially improved high-energy phosphate preservation as expected [5, 7, 8], but further improvement by glucose was not significant [10].

Glucose transport into the cell is increased by insulin in both anaerobic and aerobic states in the normothermic heart [12]. The present study examines whether the addition of insulin to an oxygenated CS containing glucose increases protection during hypothermic arrest by increased substrate availability. In addition, to elucidate the different effects of glucose and insulin when anaerobic or aerobic metabolism was maximized during arrest, and because anaerobic metabolism is likely during some part of the interval between oxygenated cardioplegic infusions, nitrogenated as well as fully oxygenated cardioplegic solutions were studied. In the isolated rat heart, we evaluated lactate production during arrest, high-energy phosphate stores at end-arrest, and functional recovery. Glycogen was also measured, in the hope of better un-

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Table 1. Composition of Solutions

Component	Krebs-Henseleit Bicarbonate Buffer	Base Cardioplegic Solution[a]
Na^+ (mEq/L)	143.0	109.3
K^+ (mEq/L)	5.9	20.0
Ca^{2+} (mEq/L)	2.4	1.4[b]
Mg^{2+} (mEq/L)	2.4	. . .
Cl^- (mEq/L)	125.1	103.3
HCO_3^- (mEq/L)	25.0	27.0
$H_2PO_4^-$ (mEq/L)	1.2	. . .
SO_4^{2-} (mEq/L)	2.4	. . .
Mannitol (mmol/L)	. . .	54.9
Glucose (mmol/L)	11.1	[a]

[a] One milliliter of 1.0 N HCl is included in the formulation of the base cardioplegic solution. The solution was modified in the different experimental groups by the addition of 28 mmol/L glucose or sucrose, equilibration with 98% O_2/2% CO_2 or 98% N_2/2% CO_2, and addition of insulin (10.0 IU/L) where appropriate, as detailed in the text. [b] Approximately 1.4 mEq/L of calcium, added as calcium chloride, was included to produce a measured ionized Ca^{2+} of 0.5 mmol/L in the cardioplegic solution in all experimental groups.

derstanding the observed benefit of glucose in oxygenated CS [10]. Multidose infusions and deep hypothermia (8° ± 2°C) were employed to simulate clinical practice.

Material and Methods

To permit examination of the effects of the presence or absence of oxygenation, the presence or absence of glucose, and the presence or absence of insulin, the investigation used eight CSs. Specifically, the CS contained either 28 mmol/L glucose or 28 mmol/L sucrose as an osmotic control, with or without 10 IU/L insulin, and was equilibrated with a mixture of 2% carbon dioxide for pH control and either 98% oxygen or 98% nitrogen.

Preparation and Protocol

Male Sprague-Dawley rats weighing 250 to 420 g were anesthetized intraperitoneally with sodium pentobarbital (65 mg/kg) and given 100 units of heparin intravenously. Beating hearts were excised and placed in ice-cold Krebs-Henseleit buffer (Table 1). The heart was then immediately mounted on a perfusion apparatus [13] and perfused through the aortic root at a pressure of 100 cm H_2O for 10 minutes by the method of Langendorff (retrograde perfusion) with the same buffer at 37°C, oxygenated with 95% O_2 and 5% CO_2. The experimental protocol is displayed in Figure 1.

During the period of Langendorff perfusion, the pulmonary artery was incised to allow free coronary venous drainage and for insertion of a thermocouple probe into the right ventricle to monitor myocardial temperature continuously. The left atrium was cannulated through a pulmonary vein, and a working heart preparation was established by perfusing the left atrium with warm oxygenated Krebs-Henseleit buffer at a pressure of 16 cm H_2O. The left ventricle ejected against a pressure of 95 cm H_2O into a recirculating aortic column. Aortic flow was measured in the aortic column by a variable-area flow meter (Model 1100; KDG Flowmeters, Burgess Hill, Sussex, England) that had been calibrated by timed volumetric collections. Coronary flow was measured by timed volumetric collection of effluent fluid from the pulmonary artery. Heart rate was obtained from strip chart recordings of aortic pressure. Aortic flow, coronary flow, and heart rate were measured at 5-minute intervals during a 15-minute prearrest stabilization period, and the final measurements were taken as the prearrest control values. Hearts with an aortic flow less than 40 mL/min, an apparent coronary flow greater than 24 mL/min, or a heart rate less than 240 beats/min were rejected from the study as possibly damaged during preparation. Fewer than 10% of hearts were rejected for these reasons.

The heart was then rendered globally ischemic by clamping the left atrial and aortic lines. This was immediately (at most 1 or 2 seconds delay) followed by the infusion of 15 mL of cold hyperkalemic crystalloid CS (see Table 1) at a pressure of 55 mm Hg through a side-arm on the aortic cannula to induce myocardial arrest. Subsequently, 10 mL of CS was given every 15 minutes for 2 hours in the same manner. During arrest, the left atrium was vented by opening a fluid-filled catheter on a side-arm of the left atrial cannula to air, with the level of the open end adjusted so that no air entered the heart. With each CS infusion, effluent CS was collected for measurement of lactate. Also, the duration of each infusion was noted. Because the cardioplegic solution level in the reservoir supplying the aortic cannula changed little during each infusion, infusion pressure was almost constant. Coronary flow drained freely from the right side of the

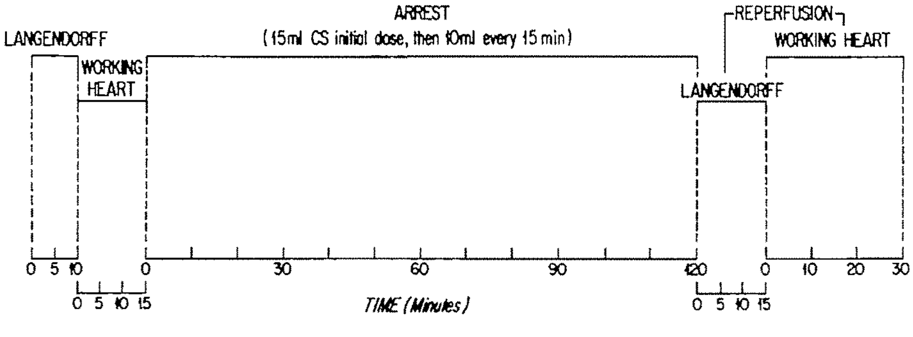

Fig 1. Experimental protocol. (CS = cardioplegic solution.)

heart, so that coronary venous pressure was near atmospheric. Therefore, mean coronary vascular resistance during each infusion was proportional to the reciprocal of coronary flow, that is, to infusion duration divided by infusion volume.

The CS was continuously bubbled with the appropriate gas in a water-jacketed reservoir supplying the side-arm on the aortic cannula. Oxygenation provides an oxygen tension greater than 800 mm Hg when measured at 37°C, the upper limit of the measurement. Oxygenated CSs had an average pH of 7.40 ± 0.005 and a carbon dioxide tension of 36.4 ± 0.5 mm Hg measured at 37°C, whereas nitrogenated CSs had a pH of 7.41 ± 0.004, a carbon dioxide tension of 35.0 ± 0.3, and an oxygen tension of 42.5 ± 1.1 mm Hg. Insulin levels in affluent and effluent CS samples, measured in several hearts, were 2,625 ± 180 and 2,460 ± 172 μU/mL, respectively. These levels demonstrated that an insulin concentration 100 times greater than the normal physiological range was delivered to the heart.

Sixteen hearts were arrested with each solution; 8 of these were freeze-clamped for assay of myocardial metabolites after 1 hour of arrest, and the remaining 8 after 2 hours of arrest. Myocardial lactate production during arrest was measured in all these hearts. In parallel studies, 8 additional hearts were freeze-clamped at each of three times in the protocol: immediately after opening the chest (ie, killed immediately), after 10 minutes of Langendorff perfusion, and at prearrest. These hearts were assayed for adenine nucleotides, phosphocreatine (PCr), and glycogen.

After arrest, a further 7 to 12 hearts arrested with each solution were reperfused with Krebs-Henseleit buffer at 37°C in the Langendorff mode for 15 minutes, simulating total cardiopulmonary bypass with maintained coronary perfusion. Coronary flow, heart rate, and temperature were recorded every 5 minutes. The working mode was then reestablished for 30 minutes with measurements of aortic flow, coronary flow, heart rate, and temperature obtained every 5 minutes. Cardiac output was calculated by adding aortic and coronary flows. Recoveries of cardiac output, aortic flow, coronary flow, and heart rate were calculated as percentages of their respective prearrest values.

An additional control group contained hearts in which arrest was omitted. These hearts were sequentially subjected to 10 minutes of Langendorff perfusion, 15 minutes in the working mode, 15 minutes of Langendorff perfusion, and 30 minutes in the working mode.

The reservoirs and tubing of the perfusion apparatus and a chamber surrounding the heart were water-jacketed for temperature control. Water at an appropriate temperature was supplied by pump circulators with thermostats. Myocardial temperature was maintained at 37° ± 0.2°C during prearrest and reperfusion periods and at 8° ± 2°C during arrest.

Myocardial Metabolite Assays

Hearts were freeze-clamped by compression between metal paddles precooled in liquid N_2. Adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP), and PCr contents of samples of the frozen tissue were determined by high-pressure liquid chromatography as described previously [7, 14]. The analysis was modified by the use of iced 0.6 N perchloric acid for homogenization, and neutralization of the homogenate by 1.0 mol/L potassium phosphate after 30 minutes at 4°C. Glycogen was assayed in additional frozen tissue by the hexokinase technique [15]. Heart water was determined in two samples of the remaining frozen ventricle by desiccating them at 90°C and averaging the results. The weighted averages of replicate analyses of adenine nucleotides, PCr, and glycogen determinations were expressed as nmol/mg dry weight. Total adenine nucleotides (TAN) were calculated by adding ATP, ADP, and AMP.

Myocardial Lactate Production

Coronary venous lactate was measured by the technique described by Gutmann and Wahlefeld [16] and expressed as the total produced during each CS infusion (micromoles). Lactate production in the second to eighth CS infusions was summed to give the total myocardial lactate production during these infusions.

Summary of Experimental Groups

Data on myocardial metabolites came from a total of 20 separate groups of hearts: killed immediately, 10 minutes of Langendorff perfusion, prearrest, 1 hour of arrest by each CS (eight groups), 2 hours of arrest with each CS (eight groups), and a control group. Data on hemodynamic variables came from a control group and from hearts arrested by each CS and then reperfused (eight groups involving no overlap with the groups that yielded data on myocardial metabolites).

Statistical Analysis

The statistical analysis was performed using SAS statistical software, version 5.6 (SAS Institute, Inc, Cary, NC) on a VAX 3600 computer (Digital Equipment Corp, Maynard, MA). Myocardial metabolite contents were subjected to univariate one-way analysis of variance using experimental group as the factor (20 levels). Repeated-measures analysis with experimental group as between-subjects factor (nine levels) was used to compare recovery of hemodynamic variables measured at 5-minute intervals during reperfusion; for this analysis, the variables were expressed as percentages of their respective prearrest values. As an indication of the general level of statistical power, we calculated the chance that a two-sample t test (using the pooled standard deviation from all the groups, with somewhat more than 60 degrees of freedom) would detect a difference of 20 percentage points between the underlying recovery percentages for two groups of nine hearts at a two-sided 0.05 level of significance. With a population standard deviation (σ) of ten percentage points (appropriate for recovery of coronary flow), the power would be nearly 0.99, and with $\sigma = 15$ (recovery in aortic flow or cardiac output) the power would be 0.8—lower but still satisfactory. Specific contrasts were tested if the overall F statistic was significant. Tests of the overall significance of oxygenation (ie, oxygenated versus nitrogenated solutions), the inclusion of glucose, and the inclusion of insulin used data from all groups arrested with the eight CSs. We also tested the effects of glucose and insulin at specific levels of the other factors, ie, the effects of adding glucose to CSs without insulin, of adding insulin to CSs containing glucose or sucrose, and of adding glucose and insulin together. Myocardial glycogen content (nanomoles glucose/milligram dry weight) was analyzed in the square-root scale to render the variability more nearly constant among the groups. Values of p less than 0.05 were taken to indicate statistical significance. In text and figures, data are expressed as mean ± standard error.

All animals were cared for in compliance with the "Guide for the Care and Use of Laboratory Animals" (NIH publication 85-23, revised 1985).

Results

Mean Coronary Vascular Resistance During Cardioplegic Infusions

Coronary resistance during CS infusions increased markedly in hearts given any of the nitrogenated CSs but remained low in hearts given the oxygenated CSs (Figure 2). The increase in resistance started as early as the fourth cardioplegic infusion. We [17] have previously shown that this rise in coronary vascular resistance is attributable to the development of ischemic contracture.

Myocardial Lactate Production

Regardless of CS composition, lactate production progressively increased with successive CS doses to a maximum, reached at either the third or fourth cardioplegic dose, at 30 or 45 minutes of arrest respectively, and then declined (Figure 3). By the eighth infusion, lactate production was low and equal with all CSs. Hearts arrested with nitrogenated CSs consistently produced more total lactate during arrest (summed over infusions 2 to 8) than those arrested with oxygenated CSs ($p = 0.0001$). Also, maximal lactate production was greater with nitrogenated CSs. Glucose added to the oxygenated CS had no effect on lactate production, either in individual doses of cardioplegia or when doses 2 through 8 were summed. In contrast, adding glucose to the nitrogenated CS produced a significant increase in total lactate production ($p < 0.05$). When single CS doses were considered, this effect was significant only for the second dose. Insulin in any solution had no significant effect on lactate production; the curves for insulin-containing CSs were similar to those in Figure 3 for insulin-free solutions equilibrated with the same gas.

Myocardial Adenine Nucleotide and Phosphocreatine Contents

These metabolite contents are depicted in Figure 4; the results of statistical analysis are in Table 2. Ten minutes of Langendorff perfusion had little effect on nucleotide levels compared to nucleotide levels after immediate death. Before arrest (ie, after 15 minutes of work) the ATP level was well maintained, and the AMP level decreased. A marked increase in PCr content was noted after Langendorff perfusion, followed by a decrease in the working mode. In general, the level of ATP decreased progressively during arrest from its prearrest level, whereas that

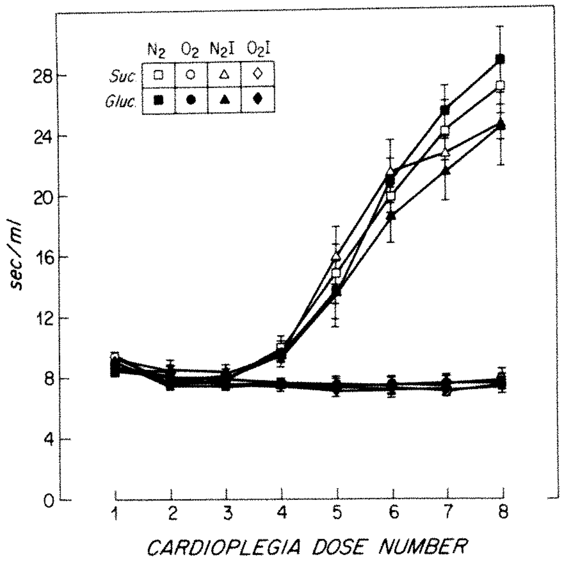

Fig 2. Mean coronary vascular resistance during each cardioplegic dose. The vertical axis shows the time for one milliliter of cardioplegic solution to flow through the heart; as explained in the Material and Methods section, this is proportional to coronary vascular resistance. Each data point for doses 1 to 4 represents 16 hearts, and for doses 5 to 8, 8 hearts. In this and subsequent figures, the symbols in the key indicate modifications to cardioplegic solution composition. The solutions contained sucrose (Suc.) *or glucose* (Gluc.) *and were equilibrated with* N_2 *or* O_2 *with or without insulin (I) as detailed in the text.* Error bars *in this and subsequent figures indicate the standard error of the mean.*

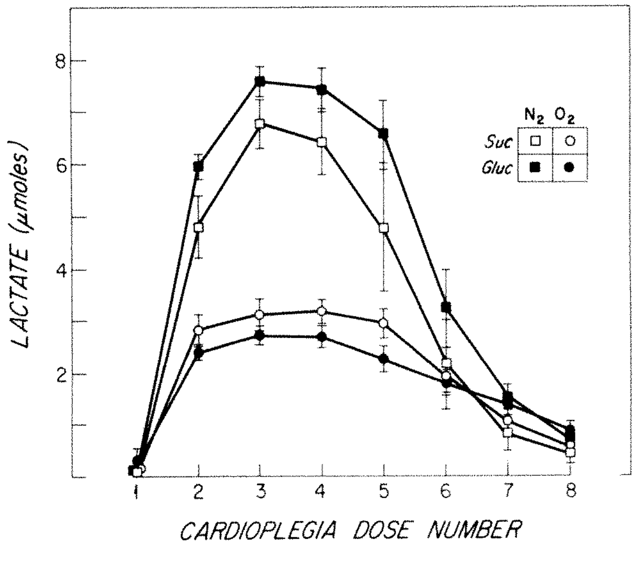

Fig 3. Lactate production in coronary venous effluent at each cardioplegic dose. Each data point for doses 1 to 4 represents 16 hearts, and for doses 5 to 8, 8 hearts.

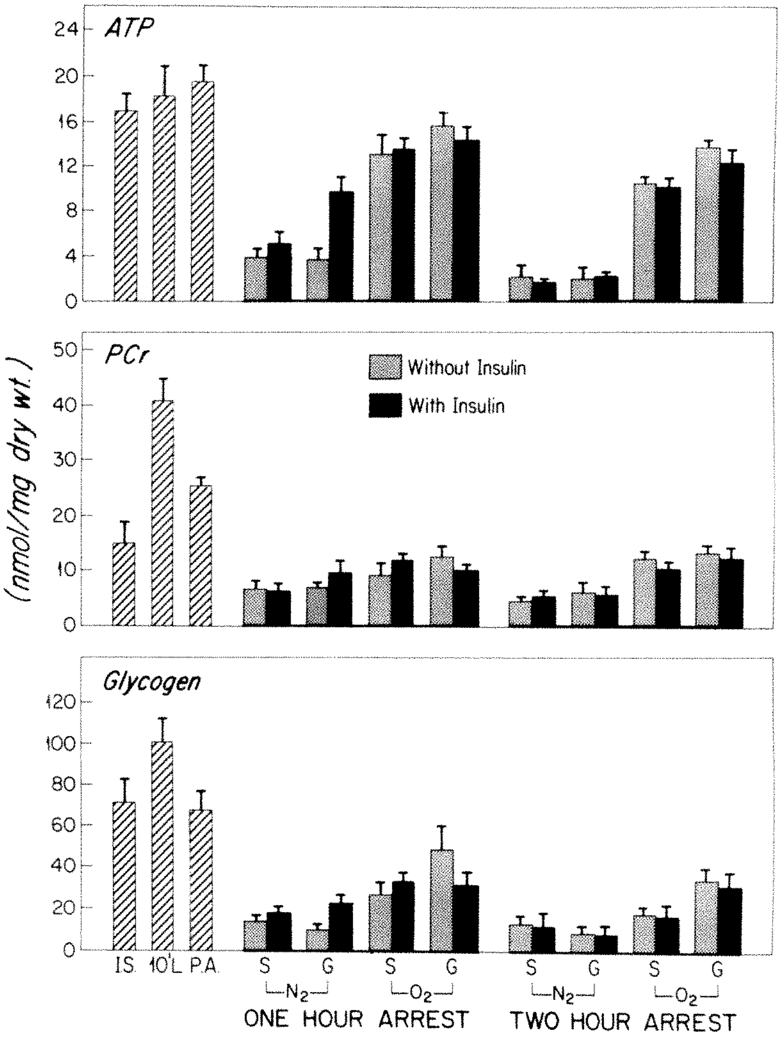

Fig 4. Myocardial metabolites expressed in nanomoles per milligram of dry weight. Upper panel: adenosine triphosphate (ATP). *Middle panel: phosphocreatine* (PCr). *Lower panel: glycogen. Each* bar *represents 8 hearts. (G = glucose;* I.S. *= immediately after opening the chest;* P.A. *= prearrest;* S *= sucrose;* 10′L *= 10 minutes Langendorff.)*

of AMP increased. The level of TAN also decreased progressively. With the nitrogenated CSs, ATP content declined to very low levels at end-arrest, consistent with ischemic contracture, as indicated by the greatly increased coronary vascular resistance (see Fig 2).

Oxygenation of the CSs, compared with nitrogenation, substantially increased the levels of ATP (see Fig 4, upper panel), ADP, TAN, and PCr (see Fig 4, middle panel) and decreased that of AMP. These overall effects of oxygenation were highly significant ($p = 0.0001$; see Table 2). Overall, glucose significantly but only modestly increased ATP and ADP levels and decreased the level of AMP (see Table 2). The addition of glucose to the oxygenated CS, however, increased ATP content at end-arrest significantly from 10.5 to 13.9 nmol/mg dry weight (see Table 2).

Overall, insulin significantly decreased the level of AMP and, to a small extent, TAN (see Table 2). In specific solutions, insulin had a significant effect only when the CS was nitrogenated and contained glucose; the addition of insulin to this CS markedly increased ATP and ADP content and decreased that of AMP at 1 hour of arrest. At end-arrest, however, hearts given this solution (as well as the other nitrogenated solutions) were in contracture, and these effects were lost as ATP, ADP, and PCr levels were greatly depleted. The greatly improved preservation of ATP content at 1 hour is due to the combination of glucose and insulin, because the level of ATP was not appreciably increased above its control value with the sucrose-nitrogen CS by either additive alone. The levels of AMP were the highest at 1 and 2 hours of arrest with the nitrogenated CS containing sucrose. Less AMP accumulated when insulin was added to this solution; this decrease in AMP largely accounted for a greater loss of TAN at 2 hours (see Table 2).

Neither glucose nor insulin had a significant effect on PCr content.

Myocardial Glycogen Content

A marked increase in glycogen stores was noted after 10 minutes of Langendorff perfusion, as compared with glycogen stores after immediate death (see Fig 4, lower panel). Glycogen stores were decreased in hearts placed in the working mode. Overall, glycogen stores were significantly better preserved by oxygenated than nitrogen-

Table 2. Myocardial Contents of Adenine Nucleotides and Phosphocreatine (nmol/mg dry weight)[a]

Time	CS	ATP	ADP	AMP	TAN	PCr	Glycogen
Killed immediately							
		16.9 ± 1.5	5.7 ± 0.6	3.2 ± 0.7	25.9 ± 1.3	15.2 ± 3.8	72.5 ± 11.1
10-minute Langendorff							
		18.3 ± 2.6	5.7 ± 0.6	5.3 ± 1.3	29.2 ± 2.6	41.0 ± 4.0	102.0 ± 11.0
Before arrest							
		19.6 ± 1.2	5.0 ± 0.4	2.5 ± 0.8	27.1 ± 1.7	25.6 ± 1.2	68.6 ± 8.9
After 1 hour of arrest							
	SN_2	3.9 ± 0.7	4.3 ± 0.4	12.3 ± 2.5	20.6 ± 2.4	6.7 ± 1.3	15.7 ± 2.0
	SN_2I	5.1 ± 0.9	4.9 ± 0.4	7.2 ± 1.2^{b}	17.2 ± 2.0	6.3 ± 1.3	19.8 ± 2.9
	GN_2	3.9 ± 0.7	4.5 ± 0.5	9.9 ± 2.1	18.3 ± 2.2	6.7 ± 0.6	10.0 ± 2.2
	GN_2I	$9.9 \pm 1.2^{c,d}$	$6.1 \pm 0.5^{e,f}$	$5.6 \pm 0.6^{b,f}$	21.7 ± 1.9	9.6 ± 1.4	24.8 ± 3.2^{e}
	SO_2	13.4 ± 1.6	6.7 ± 0.4	6.5 ± 1.6	26.6 ± 0.7	9.7 ± 1.8	27.7 ± 6.2
	SO_2I	13.8 ± 1.0	6.3 ± 0.3	5.1 ± 0.5	25.2 ± 0.9	12.1 ± 0.9	34.7 ± 4.3
	GO_2	15.8 ± 1.2	7.2 ± 0.6	4.6 ± 1.0	27.6 ± 1.2	13.0 ± 1.9	49.7 ± 11.5^{g}
	GO_2I	14.6 ± 0.9	6.8 ± 0.4	4.1 ± 0.7	25.5 ± 1.1	10.5 ± 0.8	32.3 ± 5.9
After 2 hours of arrest							
	SN_2	2.3 ± 0.9	2.9 ± 0.5	12.2 ± 3.0	17.4 ± 3.0	4.7 ± 0.7	13.8 ± 3.5
	SN_2I	1.7 ± 0.2	2.7 ± 0.3	7.3 ± 1.7^{b}	11.7 ± 1.6^{b}	5.8 ± 0.8	13.0 ± 5.2
	GN_2	2.1 ± 0.7	2.7 ± 0.1	9.5 ± 2.1	14.3 ± 2.1	6.3 ± 1.2	9.7 ± 2.3
	GN_2I	2.2 ± 0.2	3.0 ± 0.2	7.6 ± 1.8^{h}	12.8 ± 2.0	6.1 ± 1.0	8.3 ± 4.3^{h}
	SO_2	10.5 ± 0.5	6.1 ± 0.4	5.6 ± 0.6	22.2 ± 0.7	12.4 ± 1.2	18.7 ± 2.5
	SO_2I	10.2 ± 0.8	5.9 ± 0.3	5.5 ± 0.3	21.5 ± 0.8	10.6 ± 1.0	17.2 ± 6.1
	GO_2	13.9 ± 0.6^{g}	6.9 ± 0.6	4.8 ± 0.8	25.6 ± 1.1	13.7 ± 1.1	35.7 ± 5.5^{g}
	GO_2I	12.5 ± 1.1	6.1 ± 0.4	4.2 ± 0.8	22.8 ± 1.3	12.7 ± 1.7	32.7 ± 6.0
Control group							
		17.1 ± 0.9	6.7 ± 0.8	4.1 ± 0.6	27.9 ± 1.7	26.4 ± 2.8	21.5 ± 3.2
Significance of main effects (p)							
	O_2	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
	Glucose	0.0020	0.0442	0.0497	NS	NS	NS
	Insulin	NS	NS	0.0011	0.0427	NS	NS

[a] Values are mean ± standard error of the mean. Each mean represents 8 hearts. Specific comparisons are made at the same duration of arrest. [b] $p < 0.05$ versus same CS without insulin. [c] $p < 0.001$ versus same CS without insulin. [d] $p < 0.001$ versus same CS without glucose or insulin. [e] $p < 0.01$ versus same CS without insulin. [f] $p < 0.01$ versus same CS without glucose or insulin. [g] $p < 0.05$ versus same CS without glucose. [h] $p < 0.05$ versus same CS without glucose or insulin.

ADP = adenosine diphosphate; AMP = adenosine monophosphate; ATP = adenosine triphosphate; CS = cardioplegic solution; G = glucose; I = insulin; NS = not significant; N_2 = nitrogenated; O_2 = oxygenated; PCr = phosphocreatine; TAN = total adenine nucleotides.

ated CSs ($p = 0.0001$; see Table 2). The addition of glucose to the nitrogenated CS had no significant effect on glycogen stores. In contrast, the addition of glucose to the oxygenated CS resulted in significantly better maintained glycogen stores after 1 hour and 2 hours of arrest; after 2 hours, glycogen stores were about twice the level provided by the substrate-free sucrose CS (see Table 2). Insulin had no effect when added to the nitrogenated sucrose solution. On the other hand, glycogen stores, like ATP and ADP, were significantly increased after 1 hour of arrest when insulin was added to the nitrogenated CS containing glucose. Again, this effect was lost at 2 hours of arrest, when glycogen, like the high-energy phosphates, was greatly depleted in these hearts, which were in contracture. Glucose combined with insulin slightly exacerbated the profound glycogen depletion in these hearts. The addition of insulin to either oxygenated solution had no significant effect on glycogen content.

Functional Recovery

The groups of hearts arrested by the eight CSs showed no significant prearrest differences in cardiac output, aortic flow, and coronary flow (Table 3). Significant differences in heart rates among the groups were not of physiological importance. Overall, oxygenation improved recovery of cardiac output, aortic flow, and coronary flow ($p = 0.0001$; see Table 3). The effects of oxygenation on recovery of cardiac output can be seen in Figure 5. In each panel of this figure, recovery in the pair of oxygenated solutions exceeds that in the corresponding nitrogenated solutions.

Table 3. Hemodynamic Variables[a]

		Prearrest Values in Reperfused Hearts			Recovery (Percent of Prearrest Values)		
CS	n	AF (mL/min)	CF (mL/min)	CO (mL/min)	%AF	%CF	%CO
Control	8	62.5 ± 4.4	20.5 ± 1.2	83.0 ± 4.9	86.4 ± 1.7	105.5 ± 1.4	91.2 ± 1.4
SN_2	8	65.9 ± 5.0	19.1 ± 1.4	85.0 ± 6.1	22.4 ± 6.0	64.9 ± 3.9	31.9 ± 4.9
SN_2I	9	64.2 ± 4.6	19.2 ± 1.0	83.4 ± 4.4	28.4 ± 7.7	79.8 ± 3.7[b]	40.6 ± 6.0
GN_2	12	61.2 ± 3.2	20.0 ± 0.9	81.2 ± 3.2	21.1 ± 5.0	61.0 ± 6.1	31.4 ± 4.4
GN_2I	8	62.5 ± 3.7	19.2 ± 1.0	81.7 ± 4.4	42.7 ± 9.7[b]	72.8 ± 5.5	49.9 ± 8.5[b,c]
SO_2	9	62.1 ± 3.2	19.5 ± 0.8	81.6 ± 3.4	49.8 ± 8.3	83.1 ± 3.3	57.9 ± 7.0
SO_2I	10	61.2 ± 3.7	18.3 ± 0.7	79.5 ± 4.0	64.1 ± 8.8	78.5 ± 3.0	67.6 ± 6.8
GO_2	7	61.3 ± 3.2	18.9 ± 1.1	80.2 ± 3.8	62.8 ± 5.4	85.9 ± 4.3	68.8 ± 4.7
GO_2I	9	67.8 ± 3.2	22.1 ± 0.9	89.9 ± 3.7	73.1 ± 4.9[c]	84.3 ± 4.8	76.2 ± 3.2[c]
Significance of main effects							
O_2		. . .	. . .	. . .	0.0001	0.0001	0.0001
Glucose		. . .	. . .	. . .	NS	NS	NS
Insulin		. . .	. . .	. . .	0.0111	NS	0.0101

[a] Values are means ± standard errors. Prearrest values were obtained after 15 minutes of working heart mode. Percent recoveries were calculated as the average of the recoveries measured at 5, 10, 15, 20, 25, and 30 minutes of reperfusion in the working mode, each expressed as a percent of the respective prearrest value. Groups were compared by a one-way analysis of variance with repeated measures performed on these six measurements. [b] $p < 0.05$ versus same solution without insulin. [c] $p < 0.05$ versus same solution without glucose or insulin.

AF = aortic flow; CF = coronary flow; CO = cardiac output; CS = cardioplegic solution; other abbreviations as in Table 2.

The effect of adding glucose to the CSs did not attain statistical significance overall or in any specific solution, although there was a tendency to improved recovery when glucose was added to the oxygenated solution without insulin (see Fig 5A) or with insulin (see Fig 5D).

Overall, insulin significantly improved recovery of aortic flow and cardiac output (see Table 3; Figs 5B, 5C), although it was without parallel effect on high-energy phosphates or glycogen at end-arrest (see Table 2). Specifically, the addition of insulin to the nitrogenated glucose CS significantly improved recovery of cardiac output (see Fig 5B). When insulin was added to the oxygenated CS containing glucose, recovery of cardiac output improved significantly at 5 and 10 minutes of reperfusion (see Fig 5B; $p = 0.018$ and 0.035, respectively), but not over the entire 30 minutes of reperfusion. Although improvements in recovery of cardiac output and aortic flow attained by the separate sequential additions of glucose and insulin did not reach statistical significance, when glucose and insulin were added together to the oxygenated CS (ie, oxygenated glucose-insulin CS versus oxygenated sucrose CS) significant improvement was attained: averaged over the 30 min of reperfusion, cardiac output improved from 58% to 76% of its prearrest value, and aortic flow from 50% to 73% (see Table 3). Recovery of aortic flow, coronary flow, and cardiac output, even with this best solution, was less than in the control group, in which cardiac output during the period corresponding to reperfusion was 91% of its control value (see Table 3). Where cardiac output displayed improvement over the course of reperfusion (see Fig 5), this was largely attributable to increased aortic flow because coronary flow changed only slightly.

Hearts given the different CSs showed no significant differences in the recovery of heart rate.

Comment

The results of this study support previous work from this [5, 7, 8, 10] and other [6, 9] laboratories indicating the substantial benefits of full oxygenation of crystalloid cardioplegic solutions. Oxygenation resulted in better preservation of high-energy phosphate and glycogen levels during arrest, and prevented ischemic contracture. Also, lactate production during arrest was decreased and recovery of cardiac output, aortic flow, and coronary flow improved. This study also indicates that the addition of glucose to oxygenated CSs further improves myocardial protection: glucose significantly increased ATP levels and doubled glycogen levels after 2 hours of arrest without increasing lactate production. Glucose increased lactate production only when the cardioplegic solution was nitrogenated.

When insulin was added to the nitrogenated CS containing glucose, there was significantly better preservation of ATP, ADP, and glycogen levels after 1 hour of arrest; although contracture was not delayed and there was profound depletion of high-energy phosphates and glycogen by end-arrest, a significant increase in functional recovery of cardiac output and aortic flow occurred during reperfusion. The addition of insulin to the oxygenated CS containing glucose had no effect on the preservation of high-energy phosphates or glycogen, and it increased functional recovery significantly only during the first 10 minutes of reperfusion. When glucose and insulin together were added to an oxygenated CS, however, the

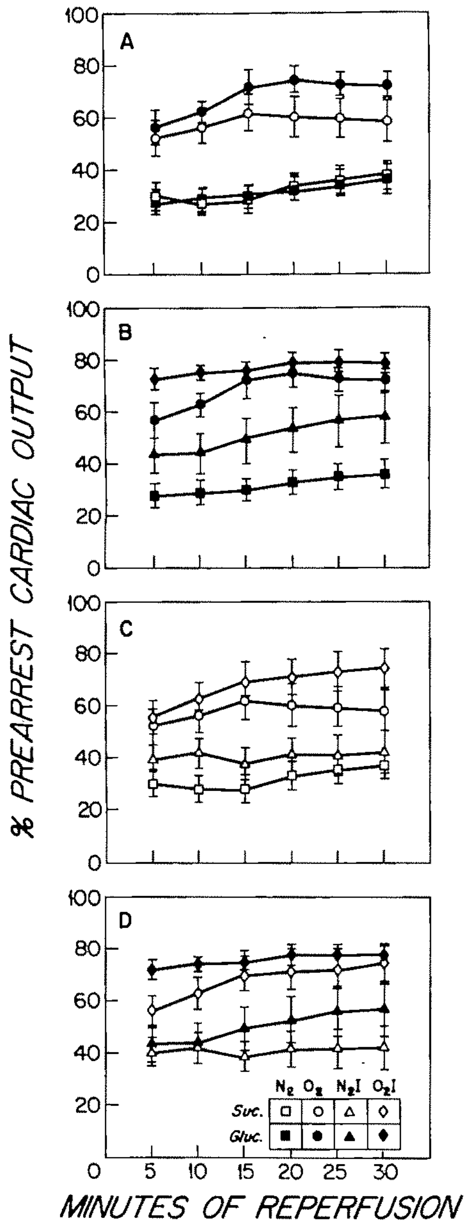

Fig 5. Recovery of cardiac output during reperfusion, expressed as a percentage of prearrest cardiac output. Each data point represents 7 to 12 hearts. (A) The insulin-free cardioplegic solutions. (B) The glucose-containing cardioplegic solutions. (C) The glucose-free cardioplegic solutions. (D) The insulin-containing cardioplegic solutions.

improvement (compared with an oxygenated sucrose CS) in recovery of both cardiac output and aortic flow attained significance throughout reperfusion.

Many reports suggest the value of glucose-insulin-potassium solutions in experimental settings [18] or perioperatively in patients undergoing cardiac operations using extracorporeal circulation [19, 20] to improve preservation of energy substrates and postoperative myocardial function. Glucose or glucose and insulin as CS additives have been studied experimentally for the most part without deliberate oxygenation of the CS and with disparate results [1–4, 21]. Whether the potential benefits of glucose as a substrate are realized may be influenced by conditions during arrest.

The ischemic myocardium depends on the anaerobic glycolytic pathway for its source of energy. For each mole of glucose that this process utilizes, 2 moles of ATP are consumed and 4 are produced for a net production of 2 moles of ATP. The end product is lactate produced from pyruvate. The administration of glucose during anoxic arrest consequently increases myocardial lactate production, and potentially decreases intracellullar pH and increases the reduced/oxidized nicotinamide adenine dinucleotide ratio, which in turn inhibits the activity of phosphofructokinase and glyceraldehyde-3-P dehydrogenase [11]. This inhibition prevents the formation of ATP anaerobically, but ATP consumption by the early steps of glycolysis may continue with consequent acceleration of ATP depletion [1]. The benefits of potential protection of glycogen stores by glucose may outweigh the deleterious effects of increased tissue lactate accumulation during ischemia [22].

Previous studies provide limited support for the concept that conditions during arrest that minimize accumulation of lactate and other deleterious glycolytic products may allow glucose to have a beneficial effect. Buckberg [23] has suggested that in the clinical setting noncoronary collateral flow and multidose administration of cardioplegic solutions act in this manner. Glucose was beneficial in studies where arrest was at a low myocardial temperature [2] or multidose cardioplegia was employed [1], but not in every instance [3, 21]. Hearse and associates [4] observed that glucose or glucose and insulin cardioplegia was detrimental and suggested that this effect was secondary to the accumulation of anaerobically produced protons and lactate. Single-dose cardioplegia and arrest at the relatively high temperature of 28°C were used in this study in the isolated rat heart. Guilbeau and co-workers [21] found in the rabbit heart that multidose as compared with single-dose cardioplegia decreased myocardial lactate accumulation, but glucose did not increase lactate accumulation under either protocol. In the studies without deliberate CS oxygenation [1–4, 21], the CS would contain an amount of oxygen intermediate between the nitrogenated and oxygenated solutions in our study [7].

By fully oxygenating the CS, we aimed to increase aerobic metabolism and decrease anaerobic metabolism in the ischemic heart. The decreased lactate production and increased ATP, PCr, and glycogen preservation observed with CS oxygenation are evidence of the success of this maneuver. In this setting of CS oxygenation, the addition of glucose did not increase lactate production, but glucose improved preservation of ATP and almost doubled glycogen stores at end-arrest. The effect on ATP content and the tendency for improved functional recovery are qualitatively similar to our previous study [10], although there the effect on ATP content did not reach significance and the effect on function did. Since the previous study [10], modifications outlined in the Material and Methods section of this report have improved the metabolite assay.

A comparison of fully oxygenated cardioplegic solutions with and without glucose and insulin by de Wit and associates [6] used a very high glucose concentration, five times that in the present study, and produced equivocal results: after 5 hours of arrest, ATP content after reperfusion was better preserved, but functional recovery was severely impaired [6].

Insulin was generally beneficial in nitrogenated and oxygenated CSs. Even with the nitrogenated CS, which stimulated substantial lactate production, the depletion of high-energy phosphates and glycogen after 1 hour of arrest was ameliorated by the addition of glucose and insulin. This finding accords with work by Weissler and colleagues [24], who demonstrated that insulin in the presence of glucose increases performance in the beating anoxic heart and improves high-energy phosphate preservation in the arrested anoxic heart. Increased uptake of exogenous glucose for glycolysis or the activation of glycogen synthase by insulin [25] may explain the sparing of glycogen stores observed at 1 hour of arrest. However, the advantages of glucose and insulin in the nitrogenated CS were insufficient to delay the development of contracture, with profound depletion of high-energy phosphates and glycogen by the end of arrest. Unexpectedly, insulin appeared to prevent excessive accumulation of AMP, presumably by stimulating the further breakdown of adenine nucleotides to simpler substances, which would be lost from the cell. With the sucrose-nitrogen CS, an extreme case without clinical parallel, there was consequent substantial loss of TAN, a deleterious effect. Also the profound glycogen depletion in the hearts in contracture was exacerbated by glucose-insulin.

Insulin increased functional recovery overall, but the mechanism is not clear; there was no parallel improvement in high-energy phosphate or glycogen preservation. The increased functional recovery seen when insulin was added to the nitrogenated CS containing glucose is obviously not due to increased high-energy phosphates or glycogen because these were profoundly depleted before reperfusion. It might be that insulin acts in some beneficial way on the cell membrane: glucose and insulin may decrease cellular potassium efflux and preserve action potential duration [26]. Another possibility is that insulin, or its effect, persists in the heart during reperfusion by insulin-free Krebs solution, acting then to increase glucose uptake and resulting in improved functional recovery.

Regardless of which CS was administered, functional recovery was less than in the control group of hearts, which were not arrested. Also, high-energy phosphates and glycogen declined during arrest. The most likely explanation is that all the CSs used in this study contained calcium, which depletes myocardial energy stores during arrest [8, 17] and impairs functional recovery [8]. Calcium appears to stress the capacity of the arrested heart to meet its energy requirements and would thereby bring out differences between cardioplegic solutions with and without substrate. Calcium was included in the cardioplegic solutions in this study for this reason and because, in the clinical setting, calcium is often included in cardioplegic formulations; if it is not included, extracellular calcium repletion by noncoronary collateral flow during arrest is probable [23].

In conclusion, this study provides further evidence that full oxygenation of a crystalloid CS permits the arrested myocardium to use aerobic metabolism, thereby greatly improving high-energy phosphate and glycogen preservation and functional recovery. The addition of glucose as a substrate to the fully oxygenated crystalloid CS further improved preservation of ATP and glycogen stores. Glucose and insulin together ameliorated the depletion of ATP, ADP, and glycogen stores by the nitrogenated CS. Although the mechanism is not clear, functional recovery was significantly improved when glucose and insulin were added together to either solution. In the extreme case of hearts in contracture after arrest by the profoundly hypoxic CS, insulin decreased the level of TAN, and glucose and insulin decreased glycogen content but enhanced functional recovery. Because the additives were otherwise beneficial, whether aerobic or anaerobic metabolism was favored during arrest, it seems probable that they would improve protection by cardioplegic solutions that were not deliberately oxygenated. Deep hypothermia and multidose cardioplegia may have minimized the potentially deleterious effects of anaerobic glycolysis. Although caution is required in applying data obtained in the isolated rat heart to the clinical situation, this study supports the use of fully oxygenated cardioplegic solutions containing glucose, and perhaps insulin, for myocardial protection, and suggests that these additives may be beneficial whether the cardioplegic solution is deliberately oxygenated or not.

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References

1. Conti VR, Kao RL. Metabolic and functional effects of carbohydrate substrate with single-dose and multiple-dose potassium cardioplegia. Ann Thorac Surg 1983;36:320–7.
2. Kao RL, Magovern GJ. Prevention of reperfusional damage from ischemic myocardium. J Thorac Cardiovasc Surg 1986; 91:106–14.
3. Salerno TA, Chiong MA. Cardioplegic arrest in pigs. Effects of glucose-containing solutions. J Thorac Cardiovasc Surg 1980;80:929–33.
4. Hearse DJ, Stewart DA, Braimbridge MV. Myocardial protection during ischemic cardiac arrest. Possible deleterious effects of glucose and mannitol in coronary infusates. J Thorac Cardiovasc Surg 1978;76:16–23.
5. Bodenhamer RH, DeBoer LWV, Geffin GA, et al. Enhanced myocardial protection during ischemic arrest: oxygenation of a crystalloid cardioplegic solution. J Thorac Cardiovasc Surg 1983;85:769–80.
6. de Wit L, Coetzee A, Kotze J, Lochner A. Oxygen requirements of the isolated rat heart during hypothermic cardioplegia. Effect of oxygenation on metabolic and functional recovery after five hours of arrest. J Thorac Cardiovasc Surg 1988;95:310–20.
7. Randolph JD, Toal KW, Geffin GA, et al. Improved myocar-

dial preservation with oxygenated cardioplegic solutions as reflected by on-line monitoring of intramyocardial pH during arrest. J Vasc Surg 1986;3:216–25.
8. Boggs BR, Torchiana DF, Geffin GA, et al. Optimal myocardial preservation with an acalcemic crystalloid cardioplegic solution. J Thorac Cardiovasc Surg 1987;93:838–46.
9. Ledingham SJM, Braimbridge MV, Hearse DJ. Improved myocardial protection by oxygenation of the St. Thomas' Hospital cardioplegic solutions. Studies in the rat. J Thorac Cardiovasc Surg 1988;95:103–11.
10. Doherty NE, Turocy JF, Geffin GA, et al. Benefits of glucose and oxygen in multidose cold cardioplegia. J Thorac Cardiovasc Surg (in press).
11. Rovetto MJ, Whitmer JT, Neely JR. Mechanisms of glycolytic inhibition in ischemic rat hearts. Circ Res 1975;37:742–51.
12. Morgan HE, Henderson MJ, Regen DM, Park CR. Regulation of glucose uptake in muscle: I. The effects of insulin and anoxia on glucose transport and phosphorylation in the isolated, perfused heart of normal rats. J Biol Chem 1961;236:253–61.
13. Yamamoto F, Braimbridge MV, Hearse DJ. Calcium and cardioplegia: the optimal calcium content for the St. Thomas' Hospital cardioplegic solution. J Thorac Cardiovasc Surg 1984;87:908–12.
14. DeBoer LWV, Ingwall JS, Kloner RA, Braunwald E. Prolonged derangements of canine myocardial purine metabolism after a brief coronary artery occlusion not associated with anatomic evidence of necrosis. Proc Natl Acad Sci USA 1980;77:5471–5.
15. Stein MW. D-Glucose, determination with hexokinase and glucose-6-phosphate dehydrogenase. In: Bergmeyer HU, ed. Methods of enzymatic analysis. New York: Academic, 1963:117.
16. Gutmann I, Wahlefeld AW. L-(+)-lactate: determination with lactate dehydrogenase and NAD. In: Bergmeyer HU, ed. Methods of enzymatic analysis. New York: Academic, 1974:1464.
17. Torchiana DF, Love TR, Hendren WG, et al. Calcium-induced ventricular contraction during cardioplegic arrest. J Thorac Cardiovasc Surg 1987;94:606–13.
18. Reikeras D, Gunnes S, Ytrehus K, Nordstrand K. Preservation of high energy phosphates during ischemic cardiac arrest with glucose. Scand J Thorac Cardiovasc Surg 1987;21:169–71.
19. Salerno TA, Wasan SM, Charrette EJP. Glucose substrate in myocardial protection. J Thorac Cardiovasc Surg 1980;79:59–62.
20. Moffitt EA, Molnar GD, Pluth JR, et al. Effects on metabolism and cardiac output of glucose-potassium solution, with and without insulin. Ann Thorac Surg 1973;15:1–15.
21. Guilbeau EJ, Moore LK, Viole AJ, et al. Effect of intermittent infusions of glucose-containing crystalloid cardioplegic solution on myocardial tissue lactic acid and recovery of contractility. J Thorac Cardiovasc Surg 1984;87:920–9.
22. Lagerstrom CF, Walker WE, Taegtmeyer H. Failure of glycogen depletion to improved left ventricular function of the rabbit heart after hypothermic ischemic arrest. Circ Res 1988;63:81–6.
23. Buckberg GD. A proposed "solution" to the cardioplegic controversy. J Thorac Cardiovasc Surg 1979;77:803–15.
24. Weissler AM, Altschuld RA, Gibb LE, et al. Effect of insulin on the performance and metabolism of the anoxic isolated perfused rat heart. Circ Res 1973;32:108–16.
25. Ramachandran C, Angelos KL, Walsh DA. Hormonal regulation of the phosphorylation of glycogen synthase in perfused rat heart. Effect of insulin, catecholamines, and glucagon. J Biol Chem 1983;258:13377–83.
26. Prasad K, Callaghan JC. Effects of glucose metabolism on the transmembrane action potential and contraction of human papillary muscle during surgical anoxia. Ann Thorac Surg 1969;7:571–81.

Phenotypic Expression of Bronchoalveolar Lavage Cells in Lung Rejection and Infection

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The differentiation of episodes of lung allograft rejection from infection continues to be a problem. Bronchoalveolar lavage (BAL) has recently gained some success in the diagnosis and management of interstitial lung disease. To assess the usefulness of BAL in differentiating between lung allograft rejection and infection, we examined the differences in cellular subsets of BAL and peripheral blood (PBL) samples in a controlled canine model of rejection or pneumonia. Single-lung allotransplants were allowed to undergo rejection by withdrawing immunosuppressive agents (n = 6). In another group of dogs (n = 5), pneumonia was induced by transbronchial injection of *Pseudomonas aeruginosa* and melted agar followed by bronchial fulguration. Cells obtained from bronchoscopic BAL and PBL samples were labeled with functionally characterized cross-reactive murine monoclonal antibodies. Transthoracic needle biopsies and transbronchial biopsies were done to assess their adequacy in examining the rejecting or infected lungs and were compared with open lung biopsies. We found the following: (1) the percentage of DT2-labeled cells was significantly higher ($p < 0.05$) in BAL samples from rejecting lungs compared with infected lungs; (2) the PBL/BAL ratio of DT2-labeled cell percentages was significantly higher in pneumonia (1.7 ± 0.3) than rejection (0.5 ± 0.2) ($p < 0.004$); (3) the percentage of E11-labeled cells in PBL samples was significantly higher ($p < 0.02$) in rejection than in infection; and (4) the ratio of WIG4 to DT2 cellular subset percentages in BAL samples from rejection (26.8 ± 9.9) was significantly lower than from infection (61.0 ± 22.9) ($p < 0.03$). Transthoracic and transbronchial biopsies did not always yield representative specimens. We conclude that differences in cellular subset composition in BAL and PBL samples from lung allotransplant rejection and pneumonia do occur. These changes may reflect the specific mechanisms of lung injury in rejection and in pneumonia. With further understanding of these changes, examination of PBL and BAL samples from lung transplant recipients will allow easier and safer differentiation of episodes of rejection from pneumonia.

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Single- and double-lung transplantations have been successful in more than 50 patients with end-stage lung disease [1, 2]. In addition, en bloc heart-lung transplantation continues to be done for refractory pulmonary hypertension with right heart failure. A difficult problem encountered in the management of such patients is the ability to successfully differentiate between episodes of acute lung rejection and infection. Treatment to date has been empirical with the administration of a high dose of steroids at the most early suspicion of the occurrence of rejection. In a heart-lung allograft, endomyocardial biopsy can indicate the development of cardiac rejection. However, it is now known that lung rejection can occur without the concomitant occurrence of detectable myocardial changes [3].

Bronchoalveolar lavage (BAL) has recently been introduced as a method with the potential to detect various causes of acute and chronic lung injury [4]. It provides direct access to cellular and fluid components within the lung without the invasiveness of biopsies and with little distortion of information by systemic changes. We postulated that BAL might provide the means to study the cellular mechanisms of injury in the lung allograft and perhaps prove useful in the differentiation between rejection and infection. In this study, we examined the phenotypic cellular changes in BAL samples under controlled experimental models of lung allograft rejection or bacterial infection.

Material and Methods

Animal Model

Left single lungs were allotransplanted into comparably sized, conditioned mongrel dogs (n = 6). The donor was fully heparinized before extraction. The recipient received a bolus of methylprednisolone (25 mg/kg intravenously) at the time of transplantation and a dose of 2.5 $mg \cdot kg^{-1} \cdot day^{-1}$ intramuscularly for the next 4 days. Cyclosporine was started on the first posttransplantation day in a dose of 7 $mg \cdot kg^{-1} \cdot day^{-1}$ orally for the next 4 days. Lung allograft rejection was allowed to occur by withholding immunosuppression on the fifth day after transplantation. The initial period of immunosuppression was essential to take the animals beyond the early postoperative period, which is recognized to manifest the so-called implantation response, a type of lung injury presumed to be caused by ischemia, reperfusion, operative handling, and interruption of lymphatics of the

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implanted lung [5]. Three to 5 days after the cessation of immunosuppression, when clinical and radiological evidence of rejection had become pronounced, the animals were subjected to bronchoscopy, BAL, lung biopsy, and peripheral blood (PBL) sampling, as detailed later. Biopsy specimens from the rejecting lungs consistently revealed grade III rejection [6].

Pneumonia was induced in the right lower lobe of normal, conditioned dogs (n = 5) by the transbronchial inoculation of 10^8 colony-forming units of *Pseudomonas aeruginosa* suspended in 10 mL of normal saline solution followed by the injection of 5 mL of melted agar. A rigid bronchoscope was used to inject the bacterial inoculum directly into the right lower lobe orifice. Fulguration of the mucosa at this site using coagulation diathermy was found to be essential to impair bacterial clearance. Without this method of narrowing the right lower lobe bronchus, the lungs were able to clear even this large bacterial inoculum with minimal evidence of the development of pneumonia. On the third day after inoculation, clinical and radiological evidence of right lower and, on one occasion, middle lobe pneumonia was detected. Bronchoscopy, BAL, lung biopsy, and PBL sampling were done. Pneumonia was confirmed by positive quantitative culture of the same bacterial species in BAL fluid and lung tissue as well as by histological examination of the specimen obtained by open lung biopsy.

Bronchoalveolar lavage was also performed in a group of normal dogs (n = 6) before any examination to obtain baseline control values of differential counts of BAL cells. Chest roentgenograms were made with the animal awake on the third day in the group with infection and on the fifth to eighth day in the group with rejection. The animals were handled under general anesthesia (sodium pentobarbital), and their care was conducted in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

On the planned study day, the dogs were anesthetized with Pentothal (thiopental sodium), 25 mg/kg intravenously. A tracheostomy was performed by cutting down on the cervical portion of the trachea with coagulation diathermy. This allows easy access of the fiberoptic bronchoscope into a more distal part of the airway, as the long cervical portion of the canine trachea occasionally limits distal access of the fiberoptic bronchoscope through an oral approach. Bleeding into the trachea was avoided to prevent contamination of the BAL samples with blood. Bronchoalveolar lavage of the rejecting or infected lungs was done by the injection of aliquots of 10 mL of phosphate-buffered saline solution up to a total of 40 mL through a small-caliber polyethylene tube wedged into a subsegmental bronchus of the left lung in the animals with rejection and the right lower lobe in the animals with pneumonia. This technique results in little loss of injected solution with the return of at least 28 mL of BAL fluid rich in peripheral bronchoalveolar cells. Contamination of the samples by central airway bleeding was also avoided. In the uncommon situation in which the specimens appeared bloody, they were discarded, and BAL was repeated after the tube was repositioned into another segmental bronchus.

After completion of BAL, a transbronchial biopsy was performed using an alligator forceps passed through the fiberoptic bronchoscope. Two bites were taken from the periphery of the rejecting lung or the right lower lobe in pneumonic animals. A fine Tru-cut transthoracic needle biopsy was done of the affected region as well. The chest was then opened through an anterolateral thoracotomy and under sterile conditions, an open lung biopsy was performed and the specimen sent for both pathological and bacteriological examination. Biopsy specimens were fixed with 40% formalin. Histological examination was done with hematoxylin and eosin stain. The animals were then killed.

Peripheral blood samples were taken as required during immunosuppression to maintain adequate renal function and cyclosporine levels. Before the termination of the study, blood samples were taken simultaneously at the time of BAL to examine them for cellular subsets.

Handling of Samples

Bronchoalveolar lavage samples were strained through coarse cotton gauze to remove mucus, which would otherwise interfere with capillary flow within the flow cytometer. The BAL and PBL samples were then subjected to total cell counts using a modified hemocytometer, and cytospinned cells were differentially counted after staining with Wright-Giemsa stains. Heparinized PBL and BAL samples were diluted 1:1 with Hanks' buffered salt solution (Grant Island Biological Co), layered over Ficoll-Hypaque, and centrifuged at 500 *g* for 40 minutes at 20°C. Mononuclear cells at the supernatant–Ficoll-Hypaque interface were removed and washed three times at 4°C with Hanks' buffered salt solution. The washed cells were resuspended at approximately 2×10^6 cells/mL before staining.

Immunofluorescence Staining

One hundred–microliter aliquots of the mononuclear cell preparation were mixed with 100 μL of Hanks' medium containing one of the seven monoclonal antibodies and incubated for 45 minutes at 4°C. The cells were then washed three times in Hanks' medium and resuspended in 200 μL of fluorescein isothiocyanate–conjugated secondary antibody for an additional 30 minutes. All staining was carried out using 1-mL Eppendorf tubes.

DLY-1 antibody has been described by Wulff and colleagues [7] to be of class IgG_{2b} and identifies a 213,000-dalton surface protein found on more than 90% of canine PBL lymphocytes, granulocytes, and monocytes and on lymphocytes stimulated by phytohemagglutinin or allogenic cells. It was found to react with only 5% to 30% of thymocytes. Treatment of canine lymphocytes with DLY-1 and complement abolished their ability to function as stimulator cells in mixed lymphocyte culture (MLC) [7].

DT-2 antibody is of subclass IgG_{2a} and identifies a 72,000-dalton protein found on 70% of mature canine PBL T-cells and 75% of puppy thymocytes. DT-2 antigen is not expressed on B lymphocytes or nonlymphoid cells. DT-

Table 1. Percentage of Bronchoalveolar Lavage and Peripheral Blood Cells Labeled With Specific Canine Monoclonal Antibodies[a]

		Rejection		Pneumonia	
Antibody	Cellular Subset	BAL	PBL	BAL	PBL
WID10	T cell	17.4 ± 18.1	11.4 ± 13.7	26.8 ± 20.3	11.3 ± 7.9
F3207	Thy-1–like	13.7 ± 20.2	11.1 ± 6.3	15.5 ± 13.9	16.4 ± 3.6
WIG4	Monocytes–CD-9 cell	9.3 ± 8.2	7.7 ± 7.2	6.2 ± 4.6	13.8 ± 14.8
E11	Supressor cell	21.8 ± 19.1	32.9 ± 10.3	8.4 ± 8.2	8.9 ± 7.1
DLY-1	T cell	7.3 ± 6.0	51.8 ± 94.7	12.9 ± 11.5	18.9 ± 12.9
DT-2	T cell	27.4 ± 15.3	14.8 ± 10.4	9.7 ± 4.2	17.7 ± 11.1

[a] Data are shown as the mean ± the standard deviation of the percentage of total cells.

BAL = bronchoalveolar lavage; PBL = peripheral blood.

2–positive cells proliferate in response to allogenic cells and mitogens but are not able to stimulate allogenic cells in MLC [8].

WIG4 antibody is an IgG_1 isotype and reacts with canine monocytes, platelets, bronchoalveolar macrophages, and a small population of Thy-1–positive lymphocytes. It does not react with granulocytes or thoracic duct cells. It also reacts with canine histiocytic cell line Mxp63 and human cell line NALM-1 (pre-B cell) and U937 (monocytic). Radioimmunoprecipitation using sodium dodecyl sulfate-polyacrylamide gel electrophoresis indicates a 24-kilodalton molecule in both canine and human cells. Canine MLC reaction is inhibited when responder cells are cytolytically treated with WIG4 monocyte-enriched cell population [9].

WID10 antibody is an IgG_1 isotype. It identifies P39 antigen, inhibits alloantigen-stimulated cells, and abrogates response to mitogens concanavalin A and phytohemagglutinin (R. Raff, Fred Hutchinson Cancer Research Center, Seattle, WA; personal communication, 1990).

F3207 antibody is an IgG_1 isotope with a molecular weight of 24,000 daltons. It is found to identify P24 antigen by sodium dodecyl sulfate–polyacrylamide gel electrophoresis and has the same mobility as pure rat Thy-1. It inhibits an assay shown previously to be directed at canine Thy-1. All thymocytes and T cells in PBL and lymph nodes were found to express Thy-1, whereas 15% of nucleated bone marrow cells are Thy-1 [10].

E11 antibody is an IgG_3 isotype. It recognizes an antigen expressed on a smaller subset of circulating T lymphocytes and on most alloantigen-stimulated suppressor lymphocytes [11].

Samples were then analyzed on a Becton Dickinson FACS Analyzer flow cytometer using a mercury lamp and filter pack system producing a wavelength of 438 nm. Results were presented as percentage of marker-positive cells ± the standard deviation. Comparison between groups for each of the monoclonal antibodies in the lung rejection group and the pneumonia group were done when possible using Student's *t* test.

Results

Bronchoalveolar lavage samples of the normal lungs yielded only a small quantity of cells (1.46 ± 0.2 × 10^5 cells/mL of lavage fluid), which consisted of 80% alveolar macrophages, 15% lymphocytes, and less than 5% polymorphonuclear leukocytes. The nontransplanted lung of the recipients consistently had total and differential counts of BAL cells similar to control values when rejection was present in the opposite lung. Both lung groups (rejection and pneumonia) showed an increase in the percentage of polymorphonuclear leukocytes in the BAL samples (rejection, 75.4% ± 53%, and pneumonia, 69.3% ± 39%). This was associated with a similar decrease in the percentage of mononuclear cells (rejection, 24.6% ± 17%, and pneumonia, 30.7% ± 35%). Peripheral blood samples similarly showed no difference between pneumonia and rejection (polymorphonuclear leukocytes: pneumonia, 74% ± 52%, and rejection, 63.3% ± 44%; mononuclear cells: pneumonia, 21.6% ± 15%, and rejection, 32.3% ± 22%).

Flow cytometric analysis of BAL and PBL cells using the previously described monoclonal antibodies (Table 1) revealed the following positive findings:

1. The percentage of DT2-labeled cells was significantly higher in BAL fluid obtained from the rejecting lungs as compared with the infected lungs ($p < 0.05$). This change was not observed in the PBL samples in rejection and pneumonia. However, the PBL/BAL ratio of DT2-labeled cell percentage was noted to be reversed when comparing rejection and pneumonia (rejection, 0.5 ± 0.2, and pneumonia, 1.7 ± 0.3; $p < 0.004$).
2. The percentage of E11-labeled cells, E11 antibody being known to recognize suppressor cells, was generally higher in BAL and PBL samples from animals with rejection compared with animals with pneumonia. However, only in PBL samples did the difference in E11-labeled cell percentage reach significance ($p < 0.02$).
3. The ratio of WIG4 to DT2 cellular subset percentages (representing mononuclear phagotype/T-cell ratio) was significantly lower in BAL fluid from the rejection group (26.8 ± 9.9) compared with that of the pneumonia group (66.0 ± 22.9) ($p < 0.03$).

Transthoracic and transbronchial biopsies revealed the correct diagnosis as documented by open lung biopsy in 2 of 11 and 5 of 11 animals, respectively. None of the

We also noted that cells that labeled with WIG4, an antibody described by the Fred Hutchinson Cancer Center group [9] as recognizing monocytes and tissue macrophages, maintained a low level of labeling in BAL and PBL samples from both the rejection and the pneumonia groups. Alveolar macrophages have been previously shown to suppress T cells in vitro and to abrogate lymphocyte blastogenesis and primary in vitro antibody response to heterologous erythrocytes [22]. The ratio of WIG4 to DT2 labeling, which may reflect the ratio of suppressor macrophages to cytotoxic T cells, was found to be significantly lower in BAL samples from the rejection group as compared with the infection group. On the other hand, WIG4 antibody was found to recognize CD-9–like antigen, which is expressed on accessory cells that are necessary for canine MLC reactivity [8]. This suggests that WIG4 labeling cells may play a more important role in rejection than infection. Whether the ratio of WIG4 to DT2 will prove to be an important marker for rejection will have to be further assessed. The changes in lymphocyte subsets observed in the rejecting lungs are unlikely to have been induced by the administration of immunosuppression, as the opposite lungs did not show similar changes. In fact, the opposite lungs consistently contained a preponderance of alveolar macrophages.

We conclude from this study that differences exist in the phenotypic expression of cells in the bronchoalveolar compartment and PBL of rejecting lung allotransplant recipients and animals with pneumonia. These differences can be identified by the performance of BAL and PBL flow cytometric analysis. Future studies may prove that phenotypic and functional analysis of BAL cells will eventually become a useful method for differentiating lung allograft rejection from infection and other forms of lung injury.

References

1. Mal H, Andreassian B, Pamela F, et al. Unilateral lung transplantation in end-stage pulmonary emphysema. Am Rev Respir Dis 1989;140:797–802.
2. Kriett JM, Kaye MP. The Registry of the International Society for Heart Transplantation: seventh official report 1990. J Heart Transplant 1990;9:323–30.
3. McGregor CGA, Baldwin JC, Jamieson SW, et al. Isolated pulmonary rejection after combined heart-lung transplantation. J Thorac Cardiovasc Surg 1985;90:623–30.
4. Raynaulds HY. Bronchoalveolar lavage—state of the art. Am Rev Respir Dis 1987;135:250–63.
5. Veith FJ, Kamholz SL, Mollenkopt FP, Montefusco CM. Lung transplantation 1983. Transplantation 1983;35:271–7.
6. Higenbottam T, Hutter JA, Stewart S, et al. Transbronchial biopsy has eliminated the need for endocardial biopsy in heart-lung recipients. J Heart Transplant 1988;7:435–9.
7. Wulff JC, Durkopp N, Aprile J, et al. Two monoclonal antibodies (DLY-1 and DLY-6) directed against canine lymphocytes. Exp Hematol 1982;10:609–19.
8. Wulff JC, Deeg HJ, Storb R. A monoclonal antibody (DT-2) recognizing canine T lymphocytes. Transplantation 1982;33:616–20.
9. Ladiges W, Deeg H, Rajantie J, et al. A monoclonal antibody which inhibits accessory cell function in the dog and recognizes a human CD9-like antigen [Abstract 9015]. Proceedings of the annual meeting of the FASEB, Las Vegas, NV, 1988.
10. McKenzie J, Fabre JW. Studies with a monoclonal antibody on the distribution of Thy-1 in the lymphoid and extracellular connective tissues of the dog. Transplantation 1981;31:275–82.
11. Szer J, Deeg HJ, Rieber P, Storb R. Monoclonal antibody to human cytotoxic-suppressor T lymphocytes cross-reacts with canine lymphocytes and inhibits cell-mediated lympholysis of canine cells. Exp Hematol 1985;13:641–64.
12. Higenbottam T, Stewart S, Penketh A, Wallwork J. Transbronchial lung biopsy for the diagnosis of rejection in heart-lung transplant patients. Transplantation 1988;46:532–9.
13. Scott JP, Higenbottam TW, Clelland CA, et al. A prospective study of 204 bronchoscopies in 52 heart-lung and lung transplant recipients using transbronchial biopsy [Abstract]. J Heart Transplant 1990;9:65.
14. Ascher N, Hoffman R, Hanto D. Cellular events within the rejecting allograft. Transplantation 1984;35:193–7.
15. Strom TB, Tilney NL, Carpenter CB, Busch GJ. Identity and cytotoxicity capacity of cells infiltrating end allografts. N Engl J Med 1975;292:1257–64.
16. Finn OJ, Micelli ML, Sanfilippo A. In vitro and in vivo human T cell repertoire in kidney allograft rejection. Transplant Proc 1988;20:155–8.
17. Shenton BK, Givan AL, Wilson RG, et al. The predictive value of immunologic monitoring in the early postoperative period in renal transplant patients. Transplant Proc 1988;20:762–3.
18. Lippolitis G, Gavazzi A, Bajani G, et al. Cytoimmunologic monitoring in heart transplant patients. Transplant Proc 1988;20:770–1.
19. Nguyen DM, Mulder DS, Shennib H. Altered cellular immune function in the atelectatic lung. Ann Thorac Surg 1991;51:76–80.
20. Molajoni ER, Bachetoni A, Cinti P, et al. Phentotypic and functional comparative analysis between infiltrating kidney transplant and peripheral blood immunocompetent cells after allograft nephrectomy. Transplant Proc 1988;20:209–10.
21. Achterrath V, Veith F. Alveolar lavage cytology in transplanted lungs. J Thorac Cardiovasc Surg 1975;69:512–9.
22. Emeson EE, Norin AJ, Kamholz KL, Veith FJ. Cytotoxic T cells and suppressor macrophages in bronchoalveolar lavage. An index to lung allograft rejection in cyclosporin-A treated dogs. Transplant Proc 1983;15:550–3.
23. Griffith B, Paradis IL, Zeevi A, et al. Immunologically mediated disease of the airways after pulmonary transplantation. Ann Surg 1988;208:371–6.
24. Zeevi A, Rabinowich H, Paradis I, et al. Lymphocyte activation in BAL from heart-lung transplant recipients. Transplant Proc 1988;20:189–92.
25. Gryzan S, Paradis IL, Hardesty RL, et al. Bronchoalveolar lavage in heart-lung transplantation. J Heart Transplant 1985;4:414–6.
26. Urban C, Wulff JC, Deeg HJ, et al. Analysis of alloreactive cytotoxic canine lymphocytes and their precursors with murine monoclonal antibodies. Transplantation 1983;35:469–73.

Growth of Tracheal Anastomoses: Advantage of Absorbable Interrupted Sutures

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Growth of the trachea after complete transection and anastomosis was studied in four groups of 1-month-old New Zealand white rabbits. The trachea was transected at the fifth cartilaginous ring and then anastomosed with continuous 6-0 polypropylene (Prolene) (group 1), interrupted 6-0 polypropylene (group 2), continuous 6-0 polydioxanone (PDS) (group 3), or interrupted 6-0 PDS (group 4). The animals were followed up for 90 to 103 days (mean follow-up, 95 days). At the time the animals were killed, body weight had increased 125% (1.2 to 2.7 ± 0.18 kg). Growth of the trachea was assessed at the time of death. Results from this study suggest that growth of a tracheal anastomosis is retarded in a growing animal model. The degree of resultant stenosis was significantly less when an absorbable suture material (PDS) and an interrupted suturing technique were used.

(Ann Thorac Surg 1991;51:636–41)

Reconstruction of the trachea may be required in pediatric patients for congenital stenosis, tracheotomy and postintubation injuries, or tracheomalacia secondary to vascular compression. Tracheal anastomosis in these instances and in pediatric heart and lung transplantation carries the risk of stenosis at the site of anastomosis. Early experimental work by Maeda and Grillo [1] and Mendez-Picon and colleagues [2] demonstrated that satisfactory growth of the trachea was possible in puppies, although narrowing did occur.

Controversy exists as to the best method of anastomosis and the choice of suture material [3–7]. Clinically, Grillo [8] found absorbable suture (Vicryl; Ethicon, Johnson & Johnson, Somerville, NJ) to be advantageous for reconstruction of the trachea because of a decrease in granulation tissue at the anastomosis. In a series of pediatric patients, Alstrup and Sorensen [9] achieved satisfactory results using interrupted Dexon (Davis + Geck, Danbury, CT) or chromic catgut sutures. Polydioxanone (PDS; Ethicon) is an absorbable suture with some theoretical advantages, including monofilament structure and predictable absorption rates, that should make it even more suitable for tracheal anastomoses [10–13].

This study was designed to compare the use of interrupted versus continuous suturing techniques and absorbable (PDS) versus nonabsorbable (polypropylene [Prolene]; Ethicon) suture material by evaluating the degree of postsurgical stenosis of the trachea in a growing animal model.

Material and Methods

One-month-old New Zealand white rabbits (mean weight, 1.2 kg) were randomized to four equal study groups ($n = 7$). The rabbits were anesthetized with intramuscular administration of xylazine (5 mg/kg) and cyclohexylamine (35 mg/kg) and allowed to breathe spontaneously without intubation. Lidocaine hydrochloride (2%) (3 mL) was injected into the tissues in the region of the neck incision to decrease discomfort.

Under sterile conditions, a vertical incision was made over the cervical trachea, the strap muscles were retracted, and the trachea was transected at the fifth cartilaginous ring. Mobilization of the trachea was limited to prevent interference with the blood supply. Internal and external dimensions in the anteroposterior and lateral planes were measured with fine calipers. Measurements were taken at the site of anastomosis (A) and at 5 mm above and 5 mm below each anastomosis. Normal (N) values were obtained as an average of those values from above and below the anastomosis. The cross-sectional area (CSA) was calculated using the formula

$$\text{CSA} = (a/2) \cdot (b/2) \cdot \pi,$$

where a = lateral diameter and b = anteroposterior diameter [14]. The tracheas were then anastomosed with continuous 6-0 polypropylene (group 1), interrupted 6-0 polypropylene (group 2), continuous 6-0 PDS (group 3), or interrupted 6-0 PDS (group 4).

The animals were electively killed after 90 to 103 days (mean follow-up, 95 days) when they had reached full size. During this period, there was a 125% increase in body weight to 2.7 ± 0.18 kg. At the time of death, tracheal measurements were taken with fine calipers. The trachea was excised and fixed in 10% buffered formalin. Silastic (Dow Corning) casts were made of each trachea,

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Table 1. Internal Diameters Measured in the Four Groups[a]

Group	I	A	N	A/N
Lateral dimension (mm)				
1: Continuous Prolene	4.4 ± 0.38	4.5 ± 1.12	6.2 ± 0.50	0.73 ± 0.15
2: Interrupted Prolene	4.3 ± 0.41	4.6 ± 0.78	6.1 ± 0.38	0.75 ± 0.12
3: Continuous PDS	4.2 ± 0.37	4.2 ± 0.57	5.5 ± 0.45	0.76 ± 0.09
4: Interrupted PDS	4.0 ± 0.45	5.5 ± 0.65[b]	6.1 ± 0.39	0.90 ± 0.11[b]
Anteroposterior dimension (mm)				
1: Continuous Prolene	3.8 ± 0.26	3.9 ± 0.99	5.4 ± 0.59	0.72 ± 0.13
2: Interrupted Prolene	3.6 ± 0.34	4.2 ± 0.72	5.1 ± 0.74	0.82 ± 0.07
3: Continuous PDS	3.7 ± 0.29	3.8 ± 0.80	4.9 ± 0.49	0.78 ± 0.11
4: Interrupted PDS	3.7 ± 0.37	4.8 ± 0.59	5.4 ± 0.53	0.89 ± 0.09[b]

[a] Data are shown as the mean ± one standard deviation. [b] Significance: $p < 0.05$, one-way analysis of variance.

A = anastomosis at death; A/N = stenosis ratio; I = initial; N = "normal" diameter at death (average of the diameter 5 mm above and 5 mm below the anastomosis).

and caliper measurements were again recorded at the site of anastomosis, 5 mm above and 5 mm below the anastomosis. Measurements from the casts were found to be more reproducible and consistent; therefore these data rather than measurements from the freshly killed specimens were used for the analysis.

Statistical analysis of the data was performed using one-way analysis of variance and the unpaired Student's *t* test. Statistical significance was defined as a probability value of 0.05 or less.

All experiments were performed in accordance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985).

Results

Four animals died intraoperatively of anesthesia-related problems. Three early deaths occurred on days 4, 8, and 13 and were due to aspiration pneumonia and infection, which could have been related to technical factors. There appeared to be no predilection for any one group and no relation to suture material. Therefore these animals were excluded from the analysis, and additional animals were used to complete the study groups. All surviving animals were killed an average of 95 days after transection and anastomosis of the trachea.

Measurements

There were no significant differences between the groups in body weight at the time of operation or death. The lateral and anteroposterior internal diameters and cross-sectional areas of the trachea were also similar at the time of transection of the trachea.

Lateral diameters were uniformly greater than anteroposterior diameters both initially and at death, a finding consistent with the recognized cross-sectional profile of the trachea. Internal diameters of both the lateral and anteroposterior dimensions for all four groups are recorded in Table 1, and calculated cross-sectional areas for all groups are shown in Table 2. Representative specimens of Silastic casts are depicted in Figure 1 (continuous polypropylene, group 1) and Figure 2 (interrupted PDS, group 4).

The A/N ratio for both diameters and the cross-sectional area of the anastomoses showed that group 4 (interrupted PDS) was significantly superior to any other group (see Tables 1, 2).

A separate analysis was performed using the A/N area ratio data for continuous (groups 1 and 3) versus interrupted technique (groups 2 and 4) and Prolene (groups 1

Table 2. Calculated Cross-Sectional Areas for the Four Groups[a]

	Area (mm^2)			
Group	I	A	N	A/N
1: Continuous Prolene	13.1 ± 1.75	14.2 ± 5.68	26.4 ± 4.68	0.54 ± 0.16
2: Interrupted Prolene	12.4 ± 1.74	15.4 ± 4.47	24.8 ± 4.90	0.62 ± 0.14
3: Continuous PDS	12.0 ± 1.89	12.5 ± 3.25	21.4 ± 3.24	0.58 ± 0.10
4: Interrupted PDS	11.9 ± 2.45	20.8 ± 3.30[b]	26.0 ± 3.99	0.80 ± 0.08[b]

[a] Data are shown as the mean ± one standard deviation. [b] Significance: $p \leq 0.05$, one-way analysis of variance.

Abbreviations are the same as in Table 1.

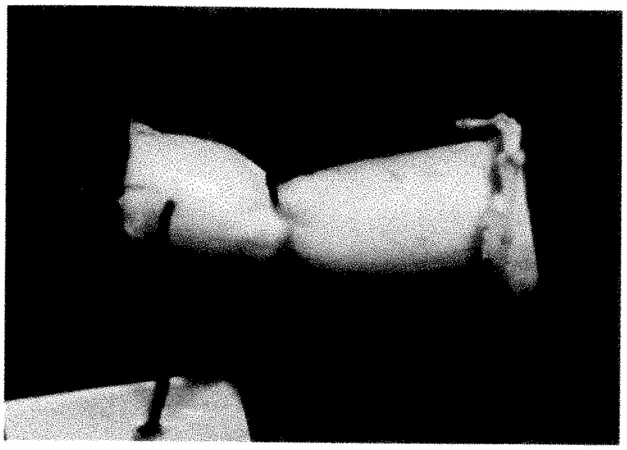

Fig 1. Silastic cast of tracheal anastomosis in an animal in group 1 (continuous Prolene). This was an extreme example of the narrowing that may occur.

Table 3. A/N Area[a, b]

Variable	Value
Continuous versus interrupted suture	
Continuous	0.55 ± 0.13
Interrupted	0.71 ± 0.14
p Value	<0.005
Prolene versus PDS	
Prolene	0.57 ± 0.15
PDS	0.69 ± 0.14
p Value	<0.025

[a] Data are shown as the mean ± the standard deviation for A/N ratio for area. [b] The p values were obtained using the one-tailed unpaired t test.

A/N = ratio of the measurement of the anastomosis at death to the normal measurement at death (average of the value 5 mm above and 5 mm below the anastomosis).

and 2) versus PDS (groups 3 and 4). Using the one-tailed unpaired t test, the differences were found to significantly favor interrupted over continuous technique ($p < 0.005$) and PDS over Prolene ($p < 0.025$) (Table 3).

Histology

Selected samples from each group were submitted for histological study. Histological sections of the tracheal anastomoses revealed persistent suture material in all four groups with an associated foreign-body giant cell reaction and a small amount of surrounding fibrosis (Figs 3, 4). PDS suture material revealed evidence of advanced hydrolysis and degradation (see Fig 4b), whereas the polypropylene material showed no apparent degeneration. Within the submucosa at the site of anastomosis, occasional small collections of mononuclear inflammatory cells (primarily lymphocytes) were seen (see Fig 4a). Focal areas of mucosal fibrosis, forming a small ridge that protruded into the lumen, were frequently present (see Fig 3a). Such protrusions in all anastomoses were always covered by respiratory epithelium. The mucosal elastica was disrupted and absent in the region of the anastomosis. Given the limited sampling, we were unable to quantitate the relative amounts of inflammation between the studied groups.

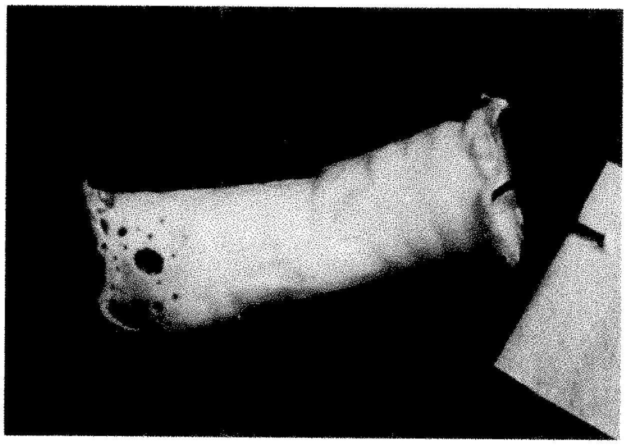

Fig 2. A fairly representative example of Silastic cast of tracheal anastomosis in an animal in group 4 (interrupted PDS). The region of the anastomosis is approximately at the midpoint of the specimen and shows only minimal deformity.

Comment

Several experimental studies [1–3, 15] demonstrating anastomotic growth of the trachea have been previously published. In 1972, Maeda and Grillo [1] reported their canine studies, which showed that growth of the trachea was possible after transection. The average growth rate was 82% of normal in the sagittal plane and 75% of normal in the coronal plane. Both nonabsorbable (4-0 Tevdek; Deknatel, Fall River, MA) and absorbable (4-0 chromic catgut) suture materials were used, but comparisons were not reported. Overlapping of the cartilaginous rings and scar formation were thought to contribute to stenosis of the anastomosis. Maeda and Grillo [1] demonstrated in a subsequent study the negative effects of tension on tracheal anastomoses after resection of part of the trachea.

Mendez-Picon and associates [2] used interrupted 4-0 silk sutures after tracheal resection in puppies, and although there were 5 long-term survivors with satisfactory results, 3 animals died early with fibrotic stenosis. Overlapping of the cartilaginous rings again was considered to be a prime factor in the development of stricture at the anastomosis. In a study using pigs, Murphy and coworkers [3] reported that overlapping of the cartilages may be disadvantageous and that a two-layer technique was useful. They used running and interrupted Dexon on the mucosa and interrupted silk on the tracheal rings. After simple transection, the edges of the trachea in our animals were approximated so as to avoid telescoping or overlapping of the rings, although some microscopic overlapping was seen histologically.

Maeda and Grillo [1] suggested that relative elongation of the membranous portion of the trachea leads to an

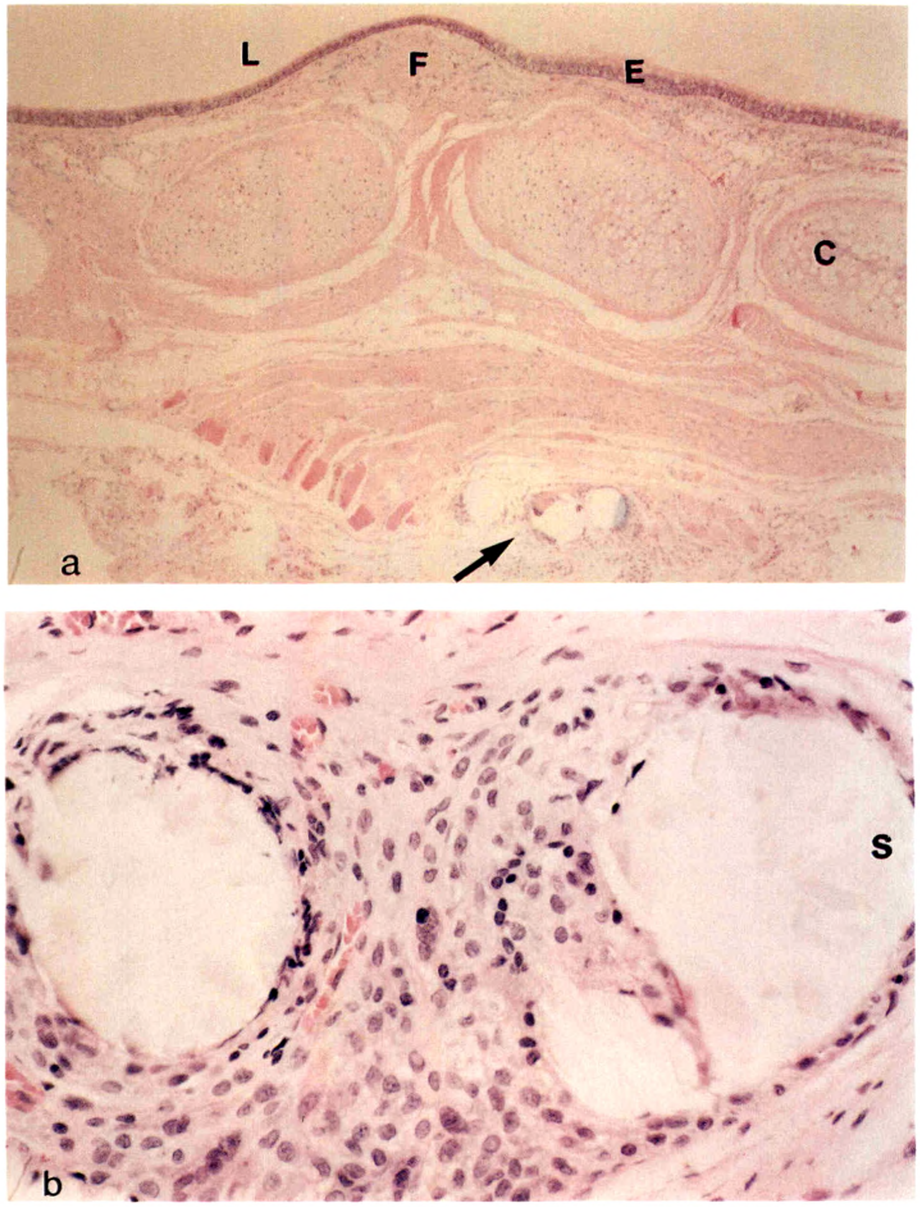

Fig 3. (a) Cross section of tracheal anastomotic site with polypropylene suture material (arrow)*. An intact respiratory epithelium* (E) *covers the luminal surface, and a focus of subepithelial fibrosis* (F) *is present. The cartilaginous rings* (C) *appear unremarkable except for focal calcification. (b) Higher-magnification photomicrograph of the suture-containing region in Figure 3a indicated by the arrow. It shows suture material* (S) *surrounded by multinuclear giant cells. The empty hole indicates the spot where another piece of suture material has fallen out of the tissue section. (a, ×50 before 32% reduction, b; ×500 before 32% reduction.)* (L = *lumen.)*

alteration in the cross-sectional shape of the trachea with growth and that the membranous area is an important region of growth. Burrington [17] demonstrated fairly uniform growth on the convex surface in the cartilaginous portion. Remodeling progressed on the concave surface. A linear relationship exists between body weight and tracheal cross-sectional area [17]. This suggests that an interrupted method of suturing or absorbable sutures would be less likely to interfere with the pattern of growth. Our study confirms this.

Nordin and Ohlsen [7], in an effort to avoid stenosis at the anastomotic site, used a Z-plasty technique with interrupted sutures. Rather than perform Z-plasty, we chose to look at the best method and the best suture material for a simple end-to-end anastomosis. Resection of the cartilaginous rings was not performed because of the risk of interrupting the blood supply of the trachea [18] and because we wanted to avoid the detrimental effects of tension on the anastomoses [16]. Lateral dissection was kept to a minimum.

Previous studies presented conflicting results between absorbable and nonabsorbable sutures. Sezeur and colleagues [6] suggested that polyglycolic acid (Dexon) and braided polyglactin (Vicryl) were not ideal and had little advantage over nylon or polypropylene. Nordin and Ohlsen [7] preferred nonabsorbable suture to polyglycolic acid and suggested there was an increased chance of separation and stenosis with absorbable suture. Their study was limited by the number of study animals. Hsieh and co-workers [15] found in a canine model and in a study similar to ours that absorbable suture (Dexon-S or Vicryl) was superior to nonabsorbable suture (nylon or Prolene) for left bronchial anastomosis. Granulomas were not found with absorbable sutures. However, the numbers in each group were insufficient for a satisfactory comparison between continuous and interrupted sutures.

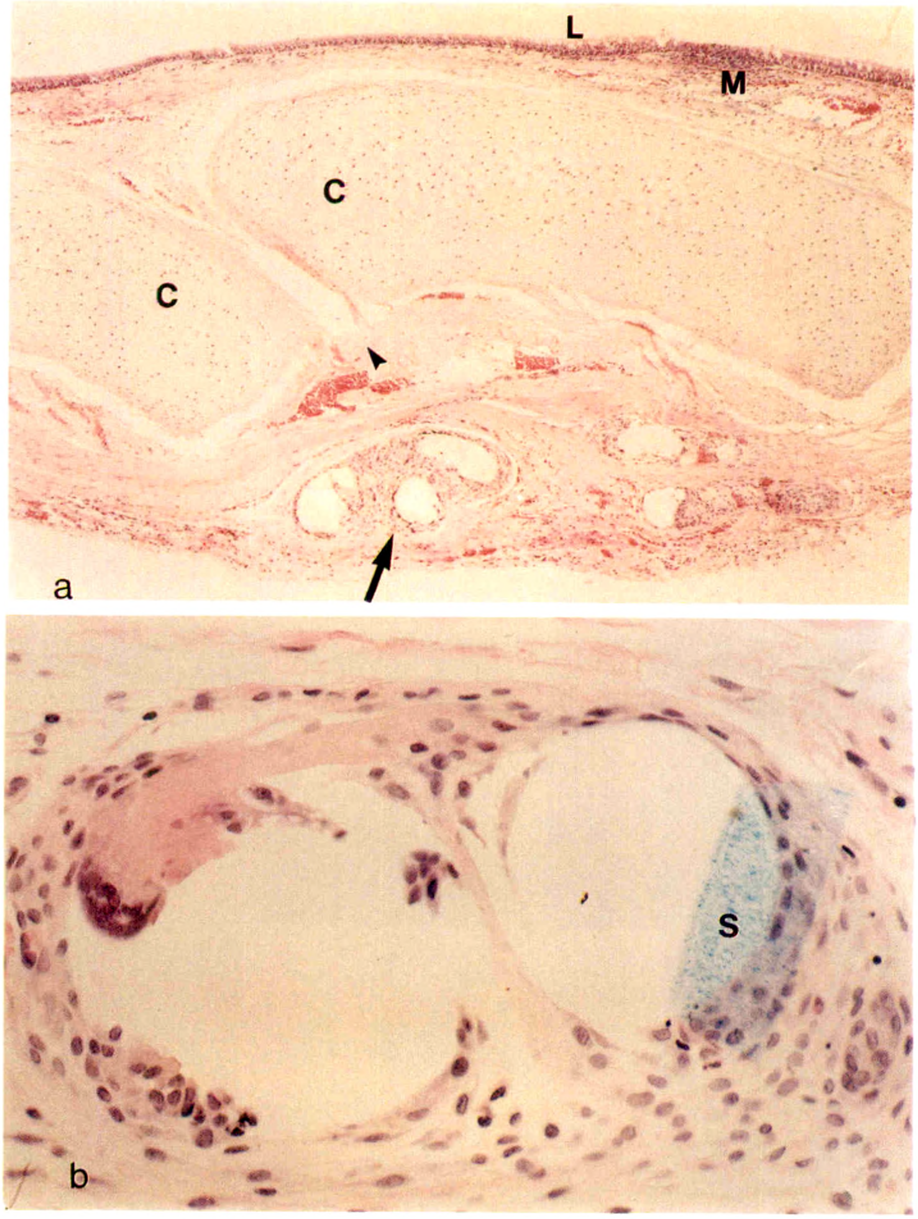

Fig 4. (a) Cross section of tracheal anastomotic site with PDS suture material (arrow). *Microscopic overlapping of the cartilaginous rings* (C) *is present* (arrowhead) *but causes little to no bulging into the lumen* (L). *One small focus of mononuclear inflammatory cell infiltrate* (M) *is present just under the respiratory epithelium. (b) Higher-magnification photomicrograph of the suture-containing region in Figure 4a indicated by the arrow. It shows a surrounding macrophage and multinuclear giant cell reaction. The enclosed suture material* (S) *is fragmented. (a, ×80 before 32% reduction, b, ×500 before 32% reduction.)*

In a study involving rabbits and dogs, Scheele and colleagues [4] found polypropylene and the absorbable sutures Dexon and Vicryl caused less reaction and less granulation and abscess formation than Mersilene (Ethicon). Dexon was successfully used in another canine study [5], which showed that by 4 months, the suture material had disappeared from the tracheal and bronchial anastomoses. Based on his extensive clinical experience, Grillo [8] thought that absorbable sutures (Vicryl) were less likely to cause granulations. Polydioxanone (PDS) theoretically has some advantages over polyglactin (Vicryl) and polyglycolic acid (Dexon). It is a monofilament, is more flexible, retains tensile strength longer, and may cause less inflammation [10–12]. Complete hydrolytic absorption of PDS was shown to occur within 26 weeks in muscle and subcuticular tissue of rats [12]. Catgut was thought to be inferior to these newer absorbable sutures [11]. PDS retains 58% of its strength at 4 weeks.

If the suture material persisted for a protracted period, it could conceivably affect growth at the anastomosis. In our study, there was still some residual suture in the anastomoses in the four PDS tracheas studied histologically, but the suture material appeared clear with moderate degradation. Hydrolytic absorption was well advanced (see Fig 4b). The inflammatory reaction was mild in all 4 PDS animals, and only 1 of them had moderate fibrosis at the suture line. Incursion into the lumen by a ridge of tissue was noted in both of the polypropylene animals (see Fig 3a). Some of this appeared to be associated with formation of scar tissue. Overlapping of the cartilages was observed in 1 of them. The number of anastomoses studied histologically is insufficient to make a comparative statement regarding the inflammatory reaction of PDS versus polypropylene suture material.

No gross evidence of abscess formation, infection, or dehiscence was seen in any of the four groups. The results in the interrupted PDS group (group 4) were significantly better than in the other three groups. Nonetheless, a satisfactory functional outcome was achieved in the majority of animals studied. Previous studies [19, 20] suggest that narrowing of the tracheal lumen by as much as 50% to 75% is required before symptomatic evidence of respiratory compromise occurs.

Formalin may have induced some postfixation shrinkage of the tracheal segments, but difficulty in measuring such small specimens in the fresh state with consistent accuracy led to the use of the Silastic cast method. The measurements of the casts were technically easier, more reproducible, and less variable and were thought to be more precise than those taken in the fresh state. Diameters measured in the fresh state at harvest and measurements from the Silastic casts after the death of the animal are noted in Table 1. Calculated areas from these data are listed in Tables 2 and 3. Because each specimen served as its own control with measurements taken above and below the anastomosis, the comparative analysis remains valid. The mean area of normal to area of anastomosis (A/N area) ratio for all groups was 0.63 with no group being less than 50% (see Table 3). Considering that all of the animals had tracheal diameters of 5 mm or less at the time of anastomosis, these results appear satisfactory. Although there was little clinical evidence of functional impairment, growth at the anastomotic site was nonetheless inhibited in all groups (see Tables 1, 2).

Conclusion

In a comparison of polydioxanone versus polypropylene and interrupted versus continuous suturing techniques, we reached the following conclusions: (1) in a growing animal model, transection of the trachea with anastomosis resulted in stenosis and retardation of growth at the anastomotic site, and (2) the use of interrupted polydioxanone sutures in tracheal anastomoses proved to be significantly superior to the other methods.

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References

1. Maeda M, Grillo HC. Tracheal growth following anastomosis in puppies. J Thorac Cardiovasc Surg 1972;64:304–13.
2. Mendez-Picon G, Hutcher NE, Neifeld J, Salzberg AM. Long-term study of tracheal growth after segmental resection in puppies. J Pediatr Surg 1974;9:615–9.
3. Murphy DA, Dunn GL, Poirier N, Martin M. Growth of tracheal anastomoses: an experimental study in weanling pigs. Ann Thorac Surg 1973;16:158–62.
4. Scheele J, Gentsch HH, Hoffmann W, Pesch HJ. Anastomosentechnik an der Trachea. Laryngol Rhinol Otol (Stuttg) 1982;61:107–14.
5. Ohata M, Idia M, Omori K, Hashimoto N, Sezai Y. Experimental study on ultrastructure of tracheobronchial anastomosis. Risho Kyobu Geka 1981;1:563–70.
6. Sezeur A, Leandri J, Rey P, Daumet P, Vouron J. Étude expérimentale du comportement des fils synthétiques à résorption lente dans les sutures trachéales. Ann Chir 1982;36: 121–5.
7. Nordin U, Ohlsen L. Prevention of tracheal stricture in end-to-end anastomosis. Arch Otolaryngol 1982;108:308–14.
8. Grillo HC. Tracheal surgery. Scand J Thorac Cardiovasc Surg 1983;17:67–77.
9. Alstrup P, Sorensen HR. Resection of acquired tracheal stenosis in childhood. J Thorac Cardiovasc Surg 1984;87: 547–9.
10. Berry AR, Wilson MC, Thomson JWW, McNair TJ. Polydioxanone: a new synthetic absorbable suture. J R Coll Surg Edinb 1981;26:170–2.
11. Lerwick E. Studies on the efficacy and safety of polydioxanone monofilament absorbable suture. Surg Gynecol Obstet 1983;156:51–5.
12. Ray JA, Doddi N, Regula D, Williams JA, Melveger A. Polydioxanone (PDS), a novel monofilament synthetic absorbable suture. Surg Gynecol Obstet 1981;153:497–507.
13. Artandi C. A revolution in sutures. Surg Gynecol Obstet 1980;150:235–6.
14. LeGal YM, Chittal SM, Wright ES. Early bronchial revascularization with an intercostal pedicle graft following canine lung autotransplantation. Can J Surg 1985;28:518–22.
15. Hsieh C, Tomita M, Ayabe H, et al. Influence of suture on bronchial anastomosis in growing puppies. J Thorac Cardiovasc Surg 1988;95:998–1002.
16. Maeda M, Grillo HC. Effect of tension on tracheal growth after resection and anastomosis in puppies. J Thorac Cardiovasc Surg 1973;65:658–68.
17. Burrington JD. Tracheal growth and healing. J Thorac Cardiovasc Surg 1978;76:453–8.
18. Salassa JR, Pearson BW, Payne WS. Gross and microscopical blood supply of the trachea. Ann Thorac Surg 1977;24:100–7.
19. Lindholm CE. Prolonged endotracheal intubation. Acta Anaesthesiol Scand [Suppl] 1970;33:1–131.
20. Ferguson DJ, Wild SJ, Wagensteen OH. Experimental resection of the trachea. Surgery 1950;28:597–619.

The Safety of Low-Dose Prednisone Before and Immediately After Heart-Lung Transplantation

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Preoperative steroid use has been considered a contraindication to heart-lung as well as lung transplantation. Moreover, most centers delay prednisone administration until 2 to 3 weeks postoperatively until airway healing is secure. We have performed 19 heart-lung transplantations and four single-lung transplantations since 1983. Five recipients (4 heart-lung, 1 single lung) had received prednisone, 5 to 40 mg daily, for 2 to 10 years preoperatively. All recipients were administered prednisone, 0.5 mg/kg daily, starting on postoperative day 1, with a taper to 0.2 mg/kg daily by 4 weeks. Minnesota antilymphocyte globulin (for 10 days), cyclosporine, and azathioprine were also employed. Bronchoscopy, lavage, and transbronchial biopsies were performed every 2 weeks for 3 months postoperatively. No patient had a serious airway complication; 2 heart-lung recipients, not on prednisone preoperatively, had a minor tracheal slough detected on bronchoscopy that resolved spontaneously. Actuarial survival after heart-lung transplantation is 84% ± 8% and 69% ± 16% at 1 year and 2 years, respectively. We conclude that prednisone commencing at a dose of 0.5 mg/kg daily from the first postoperative day is a safe practice after heart-lung transplantation. The long-term use of low-dose prednisone before heart-lung transplantation does not preclude normal tracheal healing. The safety of prednisone before and immediately after single-lung transplantation awaits confirmation by further experience.

(Ann Thorac Surg 1991;51:642–5)

Poor airway healing has historically been an important cause of death after single-lung transplantation (SLT) [1]. The early experience with double-lung transplantation has been plagued by a high incidence of major airway complications [2], although airway dehiscence and necrosis appear to be less common when a bilateral bronchial anastomotic technique is employed [2, 3]. Life-threatening airway healing problems have been less prominent in heart-lung transplantation (HLT) [4], presumably owing to collateral blood supply to the supracarinal trachea and main bronchi originating from the coronary [4] and pulmonary arteries [5, 6]. Nevertheless, tracheal anastomotic dehiscence has been an important cause of death in several series of HLT [7–9].

Because of this clinical experience and the demonstration that high-dose methylprednisolone decreases the breaking strength of bronchial anastomoses after canine lung reimplantation [10], most centers delay postoperative maintenance steroid therapy until 2 to 3 weeks postoperatively, when airway healing is believed to be secure [4, 7, 8, 11, 12]. Furthermore, patients who are taking prednisone at the time of assessment have not been considered acceptable candidates for transplantation [12].

We have performed 19 HLTs and 4 SLTs, with 1-month, 1-year, and 2-year actuarial survivals of 95% ± 5%, 84% ± 8%, and 69% ± 16%, respectively, after the former procedure. Since the inception of our program in 1983 we have used the same immunosuppressive regimen, a component of which is the institution of daily steroid maintenance therapy on the first postoperative day. In addition, we have performed HLT and SLT on patients who were taking prednisone up to the time of operation, and have not employed any technique that wraps the tracheal anastomosis after HLT. We therefore reviewed our experience with airway healing after transplantation to determine whether the preoperative and early postoperative use of steroids is a safe practice.

Patients and Methods

Nineteen HLTs were performed in 18 patients from May 1983 to September 1990. All recipients had advanced cardiorespiratory failure and were oxygen-dependent; many were not ambulatory and were wheelchair-bound owing to severe dyspnea. The 14 female and 4 male patients ranged in age from 9 to 50 years (mean, 32 ± 3 years). Their preoperative diagnoses were as follows: primary pulmonary hypertension, 10; interstitial lung disease, 3; Eisenmenger's syndrome, 2; and pulmonary thromboembolism, Kartagener's syndrome, immotile cilia syndrome, and obliterative bronchiolitis, 1 each. Al-

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Table 1. Dose and Duration of Preoperative Steroid Therapy

Diagnosis	Operation	Preoperative Daily Prednisone Dose (mg)	Duration of Prednisone Therapy (y)
Fibrosing alveolitis, right heart failure	HLT	10	5
Fibrosing alveolitis, right heart failure	HLT	5–20	2
Lymphocytic interstitial pneumonitis, right heart failure	HLT	10–40	10
Obliterative bronchiolitis after HLT	Redo HLT	10–20	2½
Sarcoidosis	SLT	10	2½

HLT = Heart-lung transplantation; SLT = Single lung transplantation.

though the majority of recipients had pulmonary vascular disease, 3 patients had diffuse interstitial lung disease with advanced clinical right heart failure. One patient in this group required high-dose dobutamine before operation to maintain hemodynamic stability. In addition, 1 recipient in whom obliterative bronchiolitis developed 2½ years after her first HLT for primary pulmonary hypertension underwent a second HLT operation.

Our recent experience with SLT includes 4 patients ranging in age from 27 to 52 years. All 4 recipients were oxygen-dependent and wheelchair-bound. The preoperative diagnoses included end-stage emphysema in 2, restrictive lung disease due to sarcoidosis in 1, and severe pulmonary hypertension due to sarcoidosis, with seemingly adequate cardiac function, in 1.

Four of the 19 HLT recipients (21%) and 1 of the SLT recipients were taking prednisone up to the time of their operation. The preoperative diagnoses of these patients, prednisone dose, and duration of steroid treatment are shown in Table 1.

Details of the operative technique and the initial postoperative care after HLT are described elsewhere [4, 13]. During the dissection in the donor as well as in the recipient, as much well-vascularized peritracheal tissue as possible was preserved. The anastomosis was performed two rings above the donor carina, using a running 3-0 polydioxanone suture for the posterior wall and multiple interrupted 3-0 polydioxanone sutures for the anterior wall. Care was taken to ensure precise mucosal approximation as well as to incorporate well-vascularized peritracheal tissue into the suture line. No tracheal anastomosis was wrapped with omentum, intercostal muscle, or pericardium.

In the group undergoing isolated lung transplantation, one right and three left SLTs were performed using standard techniques [1]. Three recipients underwent omental wrapping of the bronchial anastomosis, whereas 1 patient, who had a large amount of well-vascularized peribronchial tissue, did not receive an omental wrap.

Our postoperative immunosuppressive protocol has remained unchanged since our HLT experience began in 1983. After release of the vascular clamp, 500 mg of methylprednisolone is administered intravenously. On arrival in the intensive care unit, a regimen of Minnesota equine antilymphocyte globulin, $15\ \text{mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$, is commenced for induction immunosuppression. On the first postoperative day, administration of prednisone, $0.5\ \text{mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$, is begun; if the recipient is still intubated, an identical dose of methylprednisolone is administered. The daily prednisone dose is gradually tapered to $0.2\ \text{mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ by 4 weeks postoperatively. Cyclosporine administration is commenced on postoperative day 3 or 4, and the dose is adjusted to maintain a trough blood radioimmunoassay level of 300 to 500 ng/mL. When cyclosporine levels are therapeutic and stable, the antilymphocyte globulin regimen is discontinued, usually by the tenth postoperative day. Administration of azathioprine, 1 to $2\ \text{mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ is then begun. All recipients continue to receive cyclosporine, azathioprine, and low-dose prednisone on a long-term basis.

Since August 1988, all recipients have undergone serial follow-up bronchoscopy, bronchoalveolar lavage, and transbronchial biopsies postoperatively. These investigations have been carried out every 2 weeks during the first 3 postoperative months, then monthly until 6 months postoperatively, and then every 3 months, as well as following any clinical deterioration in the patient's respiratory status. Flexible bronchoscopy was performed using topical analgesia and low-dose intravenous fentanyl, and the examination was videotaped for future reference. After close inspection of the tracheal anastomosis, five transbronchial biopsy specimens were obtained from the upper and lower lobes of both lungs. In the SLT recipients, the healing of the bronchial anastomosis was assessed, and a similar number of biopsy specimens were taken from the transplanted lung. Episodes of lung rejection that were confirmed histologically were treated by a 3-day course of methylprednisolone, 500 mg/day. Recurrent or severe episodes of lung rejection prompted treatment with a 7- to 10-day course of OKT3, 5 mg/day intravenously.

Follow-up information was complete on every patient as of October 15, 1990. Numerical data were expressed as mean ± the standard error of the mean. The statistical significance of differences between patient groups was determined by the two-tailed t test. Actuarial survival figures and their standard errors were calculated according to the method of Cutler and Ederer [14].

Results

The 5 HLT and SLT recipients who were receiving long-term prednisone therapy preoperatively tended to be older than the recipients who were not taking steroids (41 ± 4 years versus 30 ± 3 years; $p = 0.06$) and had a higher preoperative weight (76 ± 9 kg versus 53 ± 4 kg; $p = 0.02$). There were no significant differences in sex distribution and in preoperative renal and hepatic function between the two groups.

One HLT and 2 SLT recipients died within the first 30 days postoperatively. Two additional HLT recipients died in the hospital during the first 3 postoperative months, yielding a total in-hospital mortality rate of 16% after HLT. Airway dehiscence or ischemia was not present in any of these 5 patients during the postoperative course or at autopsy. Thirteen of the 18 operative survivors of HLT are still living, and our 1-year and 2-year actuarial survival rates are 84% ± 8% and 69% ± 16%, respectively. Two SLT recipients are well 3 and 11 months postoperatively.

Of the 4 HLT recipients who were taking prednisone preoperatively, 1 died of fungal empyema and sepsis 3 months postoperatively. She had been diagnosed as having an agammaglobulinemia preoperatively in addition to lymphocytic interstitial pneumonitis and cor pulmonale, and had been receiving monthly γ-globulin injections. The other 3 HLT recipients who received prednisone preoperatively are well at 5 months, 1 year, and 4½ years postoperatively. The SLT recipient who was on long-term prednisone therapy preoperatively is well 11 months postoperatively.

Despite a program of serial postoperative bronchoscopic examinations, we have noted no episode of tracheal or bronchial dehiscence, necrosis, or stenosis in any of our HLT or SLT recipients, including those who were on long-term prednisone therapy preoperatively. In 2 HLT recipients, who were not taking prednisone before operation, a superficial tracheal slough developed in the early postoperative period, which was detected on bronchoscopy and resolved spontaneously in both cases. None of the late deaths were secondary to any complication of airway healing.

Of the 4 patients in whom diffuse bronchomalacia developed late after HLT [15], 1 was taking prednisone 10 mg/day preoperatively, whereas the other 3 had not been administered steroids until their operation (p = not significant). There were no significant differences in the daily maintenance prednisone dose postoperatively between the patients in whom bronchomalacia developed late after HLT (15 ± 4 mg/day) and those in whom this complication did not develop (12 ± 3 mg/day). Diffuse bronchomalacia occurred only in those patients in whom obliterative bronchiolitis had previously been diagnosed, and all 4 of these recipients had received multiple boluses of methylprednisolone in an attempt to arrest the progression of their pulmonary rejection late postoperatively; the *cumulative* steroid dose was therefore higher in this patient group. Nevertheless, because bronchomalacia was detected a mean of 23 ± 5 months postoperatively, there was no evidence to suggest that this complication bore any relationship to the early postoperative use of steroids.

Comment

Airway healing has historically been the Achilles heel of lung transplantation [1], and was especially problematic in the early double-lung transplant experience, in which a tracheal anastomosis was used [2]. Tracheal dehiscence and necrosis have been uncommon after HLT, probably because coronary [4] and pulmonary artery [5, 6] collaterals provide blood flow to the supracarinal trachea and main bronchi early postoperatively. Tracheal dehiscence has, however, been reported in most series of HLT [7–9], and omental wrapping of the tracheal anastomosis [7, 8] or encirclement of the trachea with the pericardial fat pad [11] has been common practice in HLT.

After SLT, omental wrapping of the bronchial anastomosis has traditionally been employed [1]. This practice is based on earlier experimental work that revealed the ability of the omentum to neovascularize the ischemic bronchus starting on postoperative day 4 [16], and to ensure adequate bronchial healing despite postoperative immunosuppressive therapy [17]. Other techniques to revascularize the bronchial anastomosis have been evaluated experimentally, including the use of intercostal muscle flaps [18], peritracheal adipose tissue [19], the internal mammary artery pedicle [20], and various methods of direct bronchial revascularization [21–23]. Because of the higher incidence of airway complications that has been reported after SLT as compared with HLT, we employed bronchial omentopexy in 3 of our 4 SLT recipients. Normal bronchial healing, however, was observed in the SLT recipient who did not receive an omental wrap, despite the fact that she required positive-pressure ventilation for more than 2 months postoperatively before recovering adequate respiratory muscle function.

Because of the deleterious effects of steroids on wound healing as well as on the breaking strength of bronchial anastomoses [10], most transplant surgeons have not until recently accepted patients who were taking prednisone at the time of assessment. Similarly, the majority of centers delay prednisone maintenance therapy until 2 to 3 weeks after lung [1, 2] and heart-lung [4, 7, 8, 11] transplantation. Experimental evidence, however, is not conclusive that steroids significantly impair bronchial anastomotic healing after bronchoplastic procedures or transplantation [22, 24]. It has been demonstrated in dogs that 2 mg/kg of prednisone daily does not increase bronchial anastomotic damage, and may indeed reduce inflammation at the anastomotic site after bronchoplasty [22]. The same investigators studied 22 dogs who had survived more than 3 weeks after left SLT, using an intussuscepting technique for the bronchial anastomosis without omental wrapping. No serious bronchial healing problems occurred, even in the 12 dogs that received prednisone as part of a cyclosporine-based immunosuppressive regimen postoperatively [24]. A recent experiment using laser Doppler velocimetry to quantitate bronchial mucosal blood flow has confirmed that prednisolone, 2 mg/kg daily, does not impair bronchial healing in dogs after bronchial division and reanastomosis as long as the peribronchial tissues are not extensively debrided [25].

A possible benefit to early postoperative steroid therapy after SLT or HLT is in providing more powerful maintenance immunosuppression during the initial postoperative weeks. Experimental work has revealed a strong correlation between lung allograft rejection and bronchial anastomotic healing [26], and gross narrowing and inflammation of the airway anastomoses in canine lung transplantation has been noted with rejection episodes [24]. A recent study has confirmed that biopsy-proven lung allograft rejection is associated with a marked decrease in the bronchial mucosal blood flow as measured by a laser Doppler flowmeter [27]. Furthermore, the degree of reduction of bronchial mucosal blood flow was correlated with the extent of mononuclear cell infiltrate around bronchial arteries and in the bronchial mucosa of the transplanted lungs [27]. These experimental observations have yet to be confirmed clinically, but enhanced immunosuppression using prednisone early postoperatively may be beneficial as long as it does not seriously impair airway healing.

Our results in clinical HLT indicate that neither the avoidance of early postoperative maintenance steroid therapy nor the use of a vascularized tracheal wrap is a requirement for normal tracheal healing. The use of maintenance prednisone, commencing at a dose of 0.5 $mg \cdot kg^{-1} \cdot day^{-1}$ from the first postoperative day, appears to be a safe practice after HLT. Furthermore, because 4 HLT recipients had uneventful tracheal healing despite the chronic preoperative use of prednisone, it does not appear justifiable to reject an otherwise suitable HLT candidate because of preoperative steroid use alone. The safety of prednisone before and immediately after SLT awaits confirmation by a larger clinical experience.

References

1. Cooper JD. Lung transplantation. Ann Thorac Surg 1989;47:28–44.
2. Patterson GA, Todd TR, Cooper JD, Pearson FG, Winton TL, Maurer J. Airway complications after double lung transplantation. J Thorac Cardiovasc Surg 1990;99:14–21.
3. Noirclerc MJ, Metras D, Vaillant A, et al. Bilateral bronchial anastomosis in double lung and heart-lung transplantations. Eur J Cardiothorac Surg 1990;4:314–7.
4. Jamieson SW, Stinson EB, Oyer PE, et al. Heart-lung transplantation for irreversible pulmonary hypertension. Ann Thorac Surg 1984;38:554–62.
5. Ladowski JS, Hardesty RL, Griffith BP. The pulmonary artery blood supply to the supracarinal trachea. Heart Transplant 1984;4:40–2.
6. Barman SA, Ardell JL, Parker JC, Perry ML, Taylor AE. Pulmonary and systemic blood flow contributions to upper airways in canine lung. Am J Physiol 1988;255:H1130–5.
7. Griffith BP, Hardesty RL, Trento A, et al. Heart-lung transplantation: lessons learned and future hopes. Ann Thorac Surg 1987;43:6–16.
8. Vouhé PR, Dartevelle PG. Heart-lung transplantation: technical modifications that may improve the early outcome. J Thorac Cardiovasc Surg 1989;97:906–10.
9. Hakim M, Higenbottam T, Bethune D, et al. Selection and procurement of combined heart and lung grafts for transplantation. J Thorac Cardiovasc Surg 1988;95:474–9.
10. Goldberg M, Lima O, Morgan E, et al. A comparison between cyclosporin A and methylprednisolone plus azathioprine on bronchial healing following canine lung autotransplantation. J Thorac Cardiovasc Surg 1983;85:821–6.
11. Emery RW, Arom KV, von Rueden T, Copeland JG. Use of the pericardial fat pad in pulmonary transplantation. J Cardiac Surg 1990;5:145–8.
12. Pearson FG. Lung transplantation. Arch Surg 1989;124:535–8.
13. Novick RJ, Menkis AH, McKenzie FN, et al. Reduction in bleeding after heart-lung transplantation: the importance of posterior mediastinal hemostasis. Chest 1990;98:1383–7.
14. Cutler SJ, Ederer F. Maximum utilization of the life table method in analyzing survival. J Chronic Dis 1958;8:699–711.
15. Novick RJ, Ahmad D, Menkis AH, et al. The importance of acquired diffuse bronchomalacia in heart-lung transplant recipients with obliterative bronchiolitis. J Thorac Cardiovasc Surg (in press).
16. Lima O, Goldberg M, Peters WJ, Ayabe H, Townsend E, Cooper JD. Bronchial omentopexy in canine lung transplantation. J Thorac Cardiovasc Surg 1982;83:418–21.
17. Saunders NR, Egan TM, Chamberlain D, Cooper JD. Cyclosporine and bronchial healing in canine lung transplantation. J Thorac Cardiovasc Surg 1984;88:993–9.
18. Legal YM, Chittal SM, Wright ES. Early bronchial revascularization with an intercostal pedicle graft following canine lung autotransplantation. Can J Surg 1985;28:518–22.
19. Legal YM, Chittal SM, Wright ES. Peritracheal membranous adipose tissue for early revascularization of the bronchial anastomosis. Can J Surg 1987;30:333–7.
20. Turrentine MW, Kesler KA, Wright CD, et al. Effect of omental, intercostal, and internal mammary artery pedicle wraps on bronchial healing. Ann Thorac Surg 1990;49:574–9.
21. Mills NL, Boyd AD, Gheranpong C. The significance of bronchial circulation in lung transplantation. J Thorac Cardiovasc Surg 1970;60:866–78.
22. Pinsker KL, Veith FJ, Kamholz SL, Montefusco C, Emeson E, Hagstrom JWC. Influence of bronchial circulation and corticosteroid therapy on bronchial anastomotic healing. J Thorac Cardiovasc Surg 1984;87:439–44.
23. Schreinemakers HHJ, Weder W, Miyoshi S, et al. Direct revascularization of bronchial arteries for lung transplantation: an anatomical study. Ann Thorac Surg 1990;49:44–54.
24. Pinsker KL, Veith FJ, Kamholz SL, Emeson EE, Norin A, Montefusco C. Bronchial anastomotic healing in canine lung allotransplants treated with cyclosporine. Transplantation 1985;40:143–6.
25. Inui K, Wada H, Yokomise H, et al. Evaluation of a bronchial anastomosis by laser Doppler velocimetry. J Thorac Cardiovasc Surg 1990;99:614–9.
26. Fujimura S, Kondo T, Handa M, et al. Histologic assessment of bronchial anastomotic healing in canine lung transplantation. J Thorac Cardiovasc Surg 1987;94:323–30.
27. Takao M, Katayama Y, Onoda K, et al. Significance of measurements of bronchial mucosal blood flow for the monitoring of acute rejection of transplanted lungs. Transplantation 1990;50:345–8.

Palliative Repair of Aortic Atresia Associated With Tricuspid Atresia and Transposition of the Great Arteries

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Successful palliative repair of aortic atresia and hypoplastic aortic arch associated with tricuspid atresia in a neonate is described. The repair consisted of reconstruction of the hypoplastic aortic arch with an equine pericardial patch, division of the patent ductus arteriosus, connection of the pulmonary artery to the aorta, implantation of the proximal part of the ascending aorta into the main pulmonary artery, and anastomosis of a polytetrafluoroethylene graft 5 mm in diameter between the right ventricular outflow tract and the central pulmonary artery, which was transferred anteriorly to the main pulmonary artery.

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Aortic atresia and hypoplastic aortic arch associated with tricuspid atresia is a rare combination of anomalies and has morphological and hemodynamic aspects similar to the hypoplastic left heart syndrome. Although various first-stage palliations for hypoplastic left heart syndrome have been performed, only a small number of the patients reach the second-stage repair, Fontan-type operation. In addition, the surgical results of the second-stage repair are still poor as the first-stage repair causes several problems mainly in the pulmonary arteries or in the aortic arch. Recently, we performed a successful first-stage repair on a neonate with a new approach under minimum circulatory arrest of the lower body. In the current report, our experience with this patient is summarized, and the advantages of this unique method of repair are discussed.

A Japanese male infant was born after an uncomplicated full-term pregnancy on September 25, 1988, weighing 3.6 kg. Soon after birth, he was noted to be cyanotic. At the regional pediatric cardiac unit, the tentative echocardiographic diagnosis of tricuspid atresia with transposition of the great arteries, aortic atresia, hypoplastic aortic arch, coarctation of the aorta, and patent ductus arteriosus was made. An infusion of prostaglandin E_2 ($0.03\ \mu g \cdot kg^{-1} \cdot min^{-1}$) was started. Angiography by retrograde injection from the radial artery showed severe hypoplasia of the ascending aorta 1 mm in diameter, narrow aortic arch and coarctation of the aorta, and patent ductus arteriosus (Fig 1).

At 13 days of age, he was referred for surgical repair to the Heart Institute of Japan, Tokyo. On admission, physical examination showed a pressure gradient of 12 mm Hg between upper and lower extremities, a grade 2/6 systolic ejection murmur along the left sternal border, and moderate hepatomegaly. The electrocardiogram showed normal sinus rhythm (140 beats/min), normal axis, left ventricular hypertrophy, and diminished right ventricular force. The chest roentgenogram showed cardiomegaly and increased pulmonary blood flow.

At the age of 18 days, the infant was taken to the operating room. The gross anatomy was compatible with the preoperative diagnosis (Fig 2). Both the pulmonary arteries were dissected out and encircled with snares. Pump perfusion was instituted with a 10F arterial cannula through the patent ductus arteriosus and with a single venous cannula in the right atrium. The hypoplastic ascending aorta was detached from the main pulmonary artery, which was transected proximal to the bifurcation. The ductus was also divided at its proximal end, and the defect in the pulmonary artery was oversewn. The proximal orifice was patch-closed with glutaraldehyde-treated equine pericardium. Then, the ascending aorta was divided and cardioplegia was induced. The proximal stump of the ascending aorta was cut open until the aortic sinus was partly exposed to make a wide anastomotic orifice and was implanted into the main pulmonary artery in an end-to-side fashion. Through the distal aortic stump, a 21F plastic needle was inserted to maintain cerebral circulation. The ductal tissue was entirely removed from the descending aorta, which was then enlarged with a semicircular patch of equine pericardium along with the coarctated segment during a 20-minute circulatory arrest of the lower body. The main pulmonary artery stump was brought up to the aortic arch by passing it under the pulmonary artery bifurcation, and wide anastomosis was made partly with an equine pericardial patch and partly

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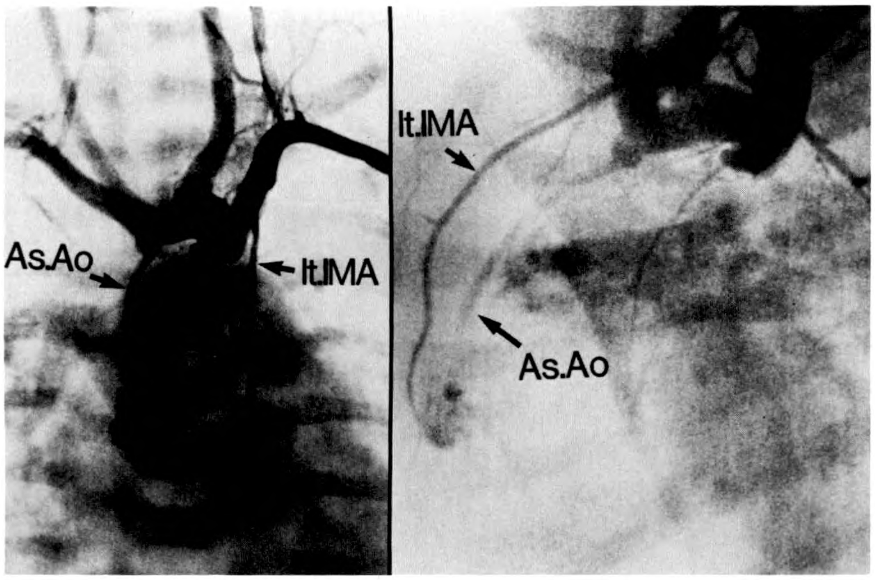

*Fig 1. Preoperative angiography by retrograde radial arterial injection showing severe hypoplasia of ascending aorta (*As. Ao*) and aortic arch. (*lt. IMA = *left internal mammary artery.)*

with an orifice in the transverse arch using 6-0 and 7-0 absorbable sutures.

After full-flow perfusion was resumed, the right atrium was opened and arterial septectomy was performed. A polytetrafluoroethylene tube 5 mm in diameter was bridged between the main pulmonary artery and the right ventricle (Fig 3). On completion of intracardiac procedure, arterial oxygen tension ranged from 32 to 35 mm Hg on an inspired oxygen fraction between 0.30 and 0.60. The postoperative course was uneventful, and he was weaned off the respirator on the 10th postoperative day and was discharged from the hospital with an arterial oxygen tension of 38 mm Hg. At 14 months of age, postoperative catheterization showed a pulmonary artery index of 180, no pressure gradient across the reconstructed arch, good coronary perfusion, mild neoaortic regurgitation, and an arterial oxygen tension of 31 mm Hg. To encourage further growth of pulmonary artery, a modified left Blalock-Taussig shunt was performed. He is currently waiting for a modified Fontan procedure.

Comment

After Norwood's initial report of successful first-stage palliation of hypoplastic left heart syndrome [1], modifications of the Norwood procedure for various lesions were proposed to overcome the early and late complications [2, 3]. Poor coronary perfusion resulting from distortion of the ascending aorta is a fatal complication. When a conduit or a homograft was used to achieve

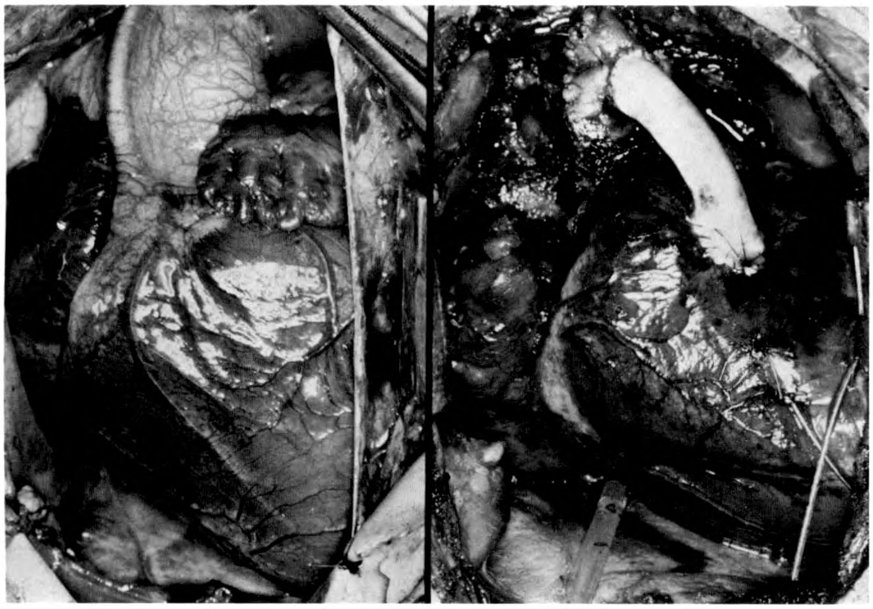

Fig 2. Intraoperative view showing severe hypoplasia of the ascending aorta and dilated main pulmonary artery (A) before operation and (B) after completion of operation.

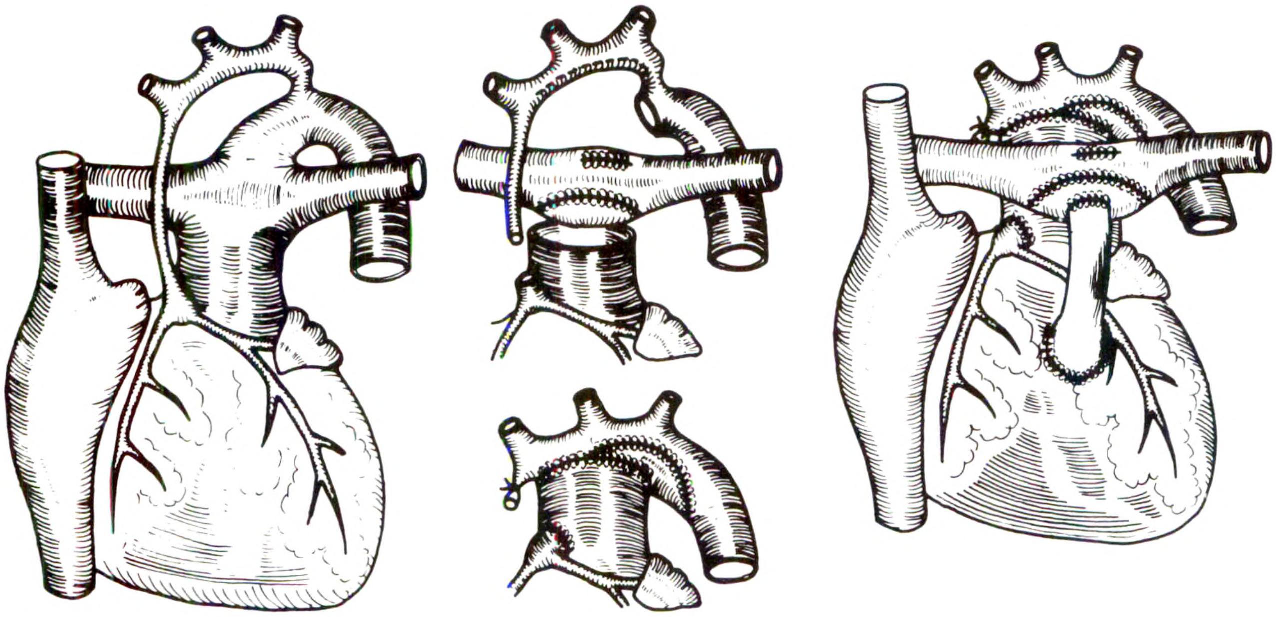

Fig 3. Operative procedure and findings.

continuity between the proximal main pulmonary artery and the aorta, minimal distortion at the most proximal point of the ascending aorta can result in poor coronary perfusion [3]. As presented here, the end-to-side anastomosis of ascending aorta just above the sinus of Valsalva can establish a "single" coronary system and can prevent its kinking or distortion. Resection of the rest of the ascending aorta makes it possible to mobilize the aortic arch and to perform anastomosis between the main pulmonary artery and the aorta without fearing kinking or distortion of hypoplastic aortic root even without a conduit and with minimal materials.

Suitability for a subsequent Fontan procedure is dependent on growth and on development of the branch pulmonary arteries centrally and pulmonary arterioles peripherally [4]. The transfer of the central pulmonary artery to a position anterior to the main pulmonary artery, which is connected to the aortic arch, can avoid compression of the central pulmonary artery by the main pulmonary artery. Furthermore, it allows us to put a shunt on the center of the central pulmonary artery. Right Blalock-Taussig shunt was reported to result in a tenting of the right pulmonary artery and uneven growth of the central pulmonary artery. In addition, this procedure is advantageous for future use of the right ventricle as in Björk's modification of Fontan procedure in a subsequent correction, as there is a usable right ventricle in this particular instance.

The shunt between the right ventricle and the pulmonary artery has different blood flow characteristics from the aortopulmonary shunt. It has only systolic flow demonstrated by postoperative Doppler study in this case, whereas continuous flow is the rule in aortopulmonary shunt. As a result, the total amount of flow should be smaller in the shunt between the right ventricle and the pulmonary artery than the conventional Blalock-Taussig shunt. Compared with the conventional shunt, therefore, it is possible to use a graft with a larger diameter for the shunt between the right ventricle and the pulmonary artery, which is advantageous for prevention of late obstruction.

References

1. Norwood WI, Lang P, Castaneda AR, Cambell DN. Experience with operations for hypoplastic left heart syndrome. J Thorac Cardiovasc Surg 1981;82:511–9.
2. Sade RM, Fyfe D, Alpert CC. Hypoplastic left heart syndrome: a simplified palliative operation. Ann Thorac Surg 1987;43:309–12.
3. Jonas RA, Lang P, Hansen D, Hickey P, Castaneda AR. First stage palliation of hypoplastic left heart syndrome. The importance of coarctation and shunt size. J Thorac Cardiovasc Surg 1986;92:6–13.
4. Pigott JD, Murphy KD, Barbar G, Norwood WI. Palliative reconstructive surgery for hypoplastic left heart syndrome. Ann Thorac Surg 1988;45:122–8.

Dynamic Cardiomyoplasty in Chronic Chagas' Heart Disease: Clinicopathological Data

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We report a 44-year-old man with chronic chagasic cardiomyopathy who underwent latissimus dorsi dynamic cardiomyoplasty and died 4 months later. The clinicopathological findings are discussed, and the literature is reviewed.

(Ann Thorac Surg 1991;51:649–51)

There has been an increasing enthusiasm in dynamic cardiomyoplasty, an electrically stimulated skeletal muscle wrapped around part of the heart, to replace or reinforce diseased myocardium [1]. A few successful clinical cases have been reported since 1985 [2]. It has been considered for the repair of defects in the ventricular wall or for the treatment of ischemic cardiomyopathy, myocardial failure due to parasitic diseases, like Chagas' heart disease, and idiopathic dilated cardiomyopathy without serious valvar insufficiency [3]. It is supposed to promote more vigorous systolic contraction and to prevent heart dilatation [3, 4]. The clinicopathological data on this procedure in humans, however, are lacking. In this report we describe a case of a patient with chronic chagasic cardiomyopathy who underwent latissimus dorsi cardiomyoplasty and died 4 months later. The heart is the most severely and frequently involved organ in the chronic phase of Chagas' disease [5].

The patient, a 44-year-old white man, was admitted to the Institute of Cardiovascular Diseases in late June 1984 because of myocardial heart failure. The diagnosis was chronic chagasic cardiomyopathy, based on the patient's history (history of bites by the insect vector), positive serology (complement-fixing antibodies), evidence of myocardial involvement, and exclusion of ischemic, hypertensive, valvar, congenital, pulmonary, and obstructive cardiomyopathies. He was maintained on a strict cardiac therapeutic program. In the interim, several tests with continuous electrocardiographic monitoring detected sinus bradycardia, ventricular escapes, idioventricular rhythm, supraventricular and ventricular extrasystoles, and ventricular paroxysmal tachycardia. In late June 1988 the patient's condition worsened despite maximal medical therapy. The chest roentgenogram showed prominent cardiomegaly. The hemodynamic studies showed mild valvar mitral regurgitation, a markedly dilated and totally hypokinetic left ventricle, with very poor function, and mild right ventricular hypokinesis with no evidence of tricuspid valve dysfunction. The coronary arteries were normal. The cardiac index determined by Fick's principle was 2.1 $L \cdot min^{-1} \cdot m^{-2}$. The patient was classified in New York Heart Association class IV.

The patient was referred for a cardiomyoplasty. Preoperative echocardiography (2 days before operation) revealed an ejection fraction of 0.31 and a heart rate of 45 beats/min. The ventricular wall thickness, the ventricular diameter and the shortening fraction were, respectively, 8 mm, 79 mm, and 0.17. In brief, the operation consisted of dissection of the left latissimus dorsi flap, keeping the axillary neurovascular bundle intact. Two intramuscular electrodes were implanted in the bundle area for muscle stimulation (Medtronic SP 5528; Medtronic, Maastricht, the Netherlands). By way of partial resection of the anterior arch of the second rib, the muscle flap was transferred to the thoracic cavity. Through a midline sternotomy the heart was exposed, and the latissimus dorsi muscle was wrapped around both ventricles in a counterclockwise fashion as viewed from the apex and fixed with interrupted sutures. A special electrode was implanted in the right ventricular wall (Medtronic SP 5548). All electrodes were coupled to a cardiomyostimulator (Medtronic SP 1005).

Synchronous muscle stimulation was begun on the 16th postoperative day. The muscle graft was put into use progressively by slowly increasing the number of pulses as well as the heart-muscle contraction ratio (3:1, 2:1, 1:1), according to a previously reported muscle transformation protocol [1]. After 8 weeks the burst frequency was 30 Hz in the 1:1 mode. Echocardiographic study 18 days after operation showed a substantial improvement of the ejection fraction from 0.31 without stimulation to 0.43 with stimulation (an increase of 0.12) and a correspondent increment of the heart rate from 45 to 70 beats/min. The ventricular wall thickness, the ventricular diameter, and the shortening fraction were, respectively, 9 mm, 74 mm and 0.18. The patient was discharged improved clinically to New York Heart Association class II on the 21st postoperative day. A substantial increase in the ejection

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fraction was detected during electrical stimulation of the muscle flap 6 weeks after operation, from 0.33 to 0.48 (an increase of 0.15). However, from 9 weeks after operation on the patient's condition deteriorated steadily, with congestive heart failure refractory to maximal medical treatment. He died 4 months after operation owing to cardiac death. In the interval, on the 5th postoperative day a serous collection developed in the latissimus dorsi muscle dissection region, which was punctured several times. To control the resultant hypoalbuminemia, plasma was administered by slow intravenous transfusion. Surgical debridement at the bed of the latissimus dorsi muscle was performed on the 54th postoperative day because of secondary infection.

At autopsy, the heart appeared grossly enlarged and dilated. The muscle flap was wrapped onto the anterior and posterior side of the heart, adherent to the myocardium, with a band of fibrous tissue between them. There was no anatomical evidence of coronary artery disease or valvar disease. The histologic examination of the myocardium showed two distinct morphological aspects: (1) severe active chronic chagasic myocarditis, characterized by cardiac muscle fibers markedly hypertrophied, diffuse foci of myocardial necrosis and degeneration with an inflammatory response composed predominantly of mononuclear cells, and striking interstitial fibrosis (Fig 1A); occasional myofibers were parasitized with leishmanial forms of *Trypanosoma cruzi* (parasitic pseudocysts), although the presence of parasites was not directly correlated with the inflammatory infiltrate (Fig 1B); and (2) diffuse subepicardial microscopic foci of myocardial cell necrosis with a cellular reaction dominated by polymorphs with mononuclear cells appearing to a minor extent (Fig 1C). Microscopic examination of the skeletal muscle showed muscle fibers with no abnormalities, except for occasional foci of atrophic myofibers and interstitial fibrosis (Fig 2A). Thin encapsulation surrounded the electrode pairs, and the surrounding muscular tissue showed myofibers with degenerative and regenerative changes, and interstitial fibrosis (Fig 2B).

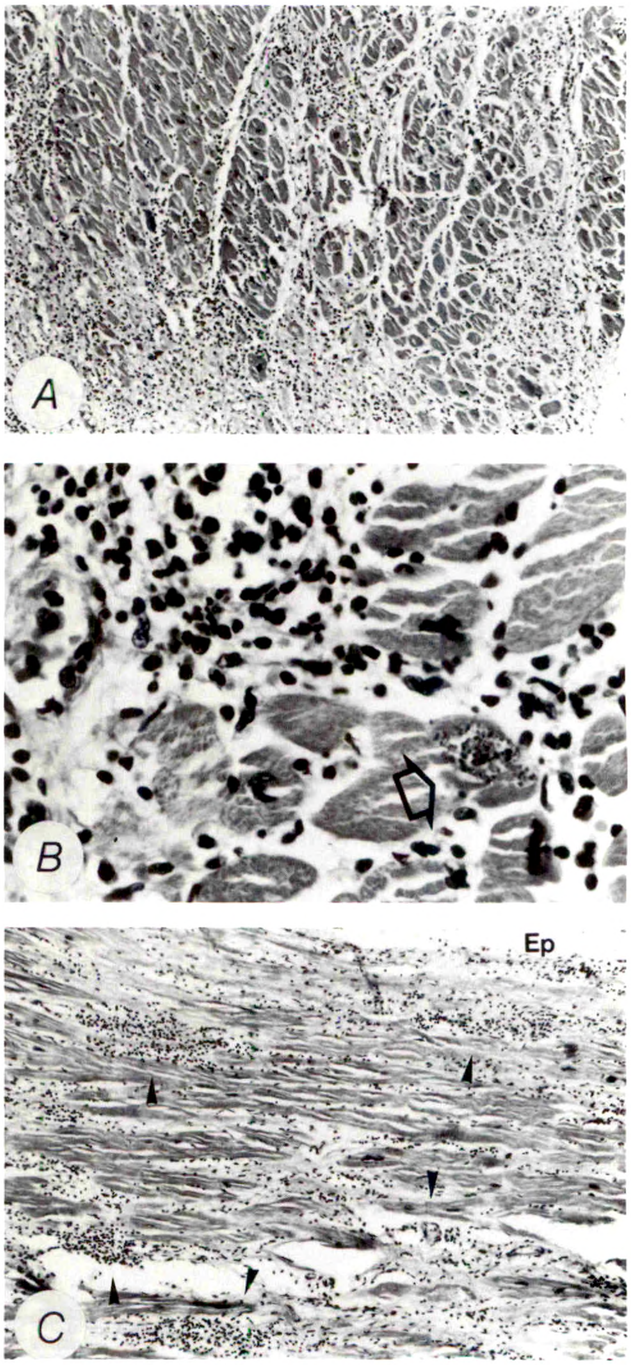

Fig 1. Myocardium. (A) Diffuse chronic myocarditis characterized by foci of myocardial necrosis and degeneration with an inflammatory response composed predominantly of mononuclear cells and interstitial fibrosis. (B) Myofiber containing parasitic pseudocyst (open arrow). *The inflammatory infiltrate is not directly correlated with the presence of parasites. (C) Scattered subepicardial microscopic foci of myocardial cell necrosis with a cellular reaction dominated by polymorphic cells with mononuclear cells appearing to a minor extent* (arrows). *(*Ep = *epicardium.) (Hematoxylin and eosin; A and C, ×85; B, ×460, all before 3% reduction.)*

Comment

The major points of this case are: first, an initial sizeable ejection fraction improvement by the synchronously paced latissimus dorsi muscle occurred, as evidenced by echocardiographic evaluation; and second, despite the initial augmented left ventricular performance, a marked deterioration of the patient's condition ensued, with refractory progressive failure of the myocardium and death. The myocardial pathological changes detected may explain the clinical course. The foci of myocardial necrosis in the subepicardial myocardium could be caused by the muscle wrap, by causing ischemia similar to constrictive pericarditis [6], although there was no clinical evidence of diastolic functional impairment. On the other hand, because the skeletal muscle showed preserved morphological structure, and fatigue resistance is the most important functional characteristic of the muscle transformation by chronic low-frequency electrical stimulation [2], it seemed that the muscle flap was not fatiguing.

Encouraging clinical results with dynamic cardiomyo-

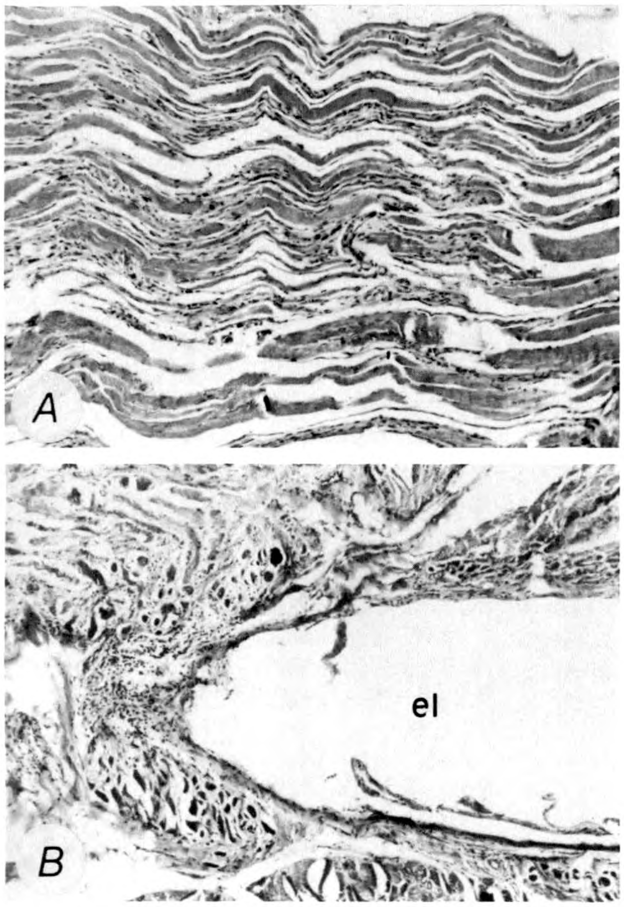

*Fig 2. (A) Skeletal muscle (latissimus dorsi). Occasional focus of atrophic myofibers and interstitial fibrosis. (B) The electrode (*el*) is surrounded by thin encapsulation. The surrounding muscular tissue shows atrophic and degenerated myofibers, and fibrosis. (Hematoxylin and eosin; ×85 before 3% reduction.)*

plasty for patients suffering from chronic Chagas' heart disease have been reported [7, 8]. The application of cardiomyoplasty in these patients has a great deal of appeal because transplantation has resulted in a very high frequency of recurrence of *T cruzi* infection with parasitemia and acute debilitation. Also, patients with active myocardial inflammation have been noted to reject at higher frequency than other transplant recipients. This case presentation correlating clinical and pathological findings sheds insight into this relatively new surgical procedure, raising a question concerning the use of such grafts in cases of markedly dilated hearts associated with severe active chronic myocarditis.

M. A. Rossi is Senior Investigator of the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq - Proc. 301109-79-6).

References

1. Carpentier A, Chachques JC. Latissimus dorsi cardiomyoplasty to increase cardiac output. In: Rábago G, Cooley DA, eds. Heart valve replacement: current status and future trends. Mount Kisco, NY: Futura, 1987:473–86.
2. Hill AB, Chiu RC-J. Dynamic cardiomyoplasty for treatment of heart failure. Clin Cardiol 1989;12:681–8.
3. Chachques JC, Grandjean P, Schwartz K, et al. Effect of latissimus dorsi dynamic cardiomyoplasty on ventricular function. Circulation 1988;78(Suppl 3):203–16.
4. Anderson WA, Anderson JS, Acker MA, et al. Skeletal muscle grafts applied to the heart. A word of caution. Circulation 1988;78(Suppl 3):180–90.
5. Rossi MA. Microvascular changes as a cause of chronic cardiomyopathy in Chagas' disease. Am Heart J 1990;120:233–6.
6. Gregory MA, Whitton ID, Cameron EWJ. Myocardial ischemia in constrictive pericarditis—a morphometric and electron microscopical study. Br J Exp Pathol 1984;65:365–76.
7. Moreira LF, Stolf NG, Bocchi EA, et al. Latissimus dorsi cardiomyoplasty in the treatment of patients with dilated cardiomyopathy. Circulation 1989;80(Suppl 2):527.
8. Molteni L, Almada HE, de Palma C, Ferreira R. Dynamic cardiomyoplasty: clinical experience. In: Chiu RC-J, Bourgeois I, eds. Transformed muscle for cardiac assist and repair. Mount Kisco, NY: Futura, 1990:189–97.

Fibrosing Mediastinitis With Coronary Artery Involvement

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This case report describes a patient with chronic fibrosing mediastinitis involving the entire intrapericardial aorta, innominate artery, and the base of the heart with involvement of the proximal segments of the coronary arteries. This finding was unsuspected before emergency coronary artery bypass grafting. Coronary stenosis due to fibrosing mediastinitis is a rare complication of fibrosing mediastinitis. Owing to the extensive fibrosis, the normal bypass, cardiac preservation, and revascularization techniques required alteration and are discussed.

(Ann Thorac Surg 1991;51:652–4)

Chronic fibrosing or sclerosing mediastinitis is an uncommon condition, usually of unknown cause, that produces marked fibrosis in the superior mediastinum. This can result in compression of adjacent mediastinal structures, most commonly the low-pressure superior vena cava but also the pulmonary arteries and veins, trachea and bronchi, esophagus, and lung [1]. The incidental finding of fibrosing mediastinitis in a patient undergoing elective coronary artery bypass grafting for atheromatous disease has been described [2].

We report a case in which the fibrosing process extended onto the epicardium to constrict the coronary vessels and resulted in the patient being seen with typical angina pectoris.

A 49-year-old man was seen with a 2-month history of angina. He had been an insulin-dependent diabetic for 12 years, had not smoked for 22 years, and had a serum cholesterol level of 4.5 mmol/L (174 mg/dL). Physical examination and chest roentgenogram were normal. At coronary angiography he had a 95% proximal stenosis in a dominant right coronary artery, two 70% stenoses in the left anterior descending artery, and a 70% narrowing of the first marginal branch of the circumflex artery. The findings were typical of atherosclerosis. The left ventricle was normal.

Percutaneous transluminal angioplasty of the right coronary lesion was attempted 3 weeks later. Despite repeated dilations there was no improvement in the right coronary artery stenosis, and the vessel occluded as a result of an ostial dissection caused by the guiding catheter recoiling from a noncompliant ascending aorta. This resulted in chest pain, which resolved after insertion and use of an intraaortic balloon pump. The patient was transferred to the operating room within 1 hour of vessel occlusion.

At operation the entire ascending aorta was found to be encased in a mass of dense, white tissue, extending superiorly around the innominate artery and inferiorly to the right ventricle and proximal right coronary artery and left anterior descending artery. Multiple biopsy specimens were taken, and frozen section examination revealed dense fibrosis but no evidence of malignancy.

Femoral artery cannulation combined with a single right atrial cannula was used to provide cardiopulmonary bypass, the right internal mammary artery was mobilized, and the right subclavian artery was exposed at the base of the neck above the fibrous mass. The patient was cooled to 25°C, the perfusion pressure was reduced, the left ventricle was vented through the left atrium, and the distal anastomoses were performed with a fibrillating, perfused heart. Vein grafts were applied to the left anterior descending artery and circumflex arteries, and the right internal mammary artery was anastomosed to the right coronary artery immediately proximal to the acute margin. The walls of the coronary arteries were not atherosclerotic. During rewarming the vein graft to the left anterior descending artery was anastomosed end-to-side to the circumflex vein graft. A single anastomosis to the right subclavian artery was then performed using an exclusion clamp (Fig 1). The patient was weaned from bypass easily.

Histological examination of the biopsy specimens revealed dense hyaline connective tissue with a patchy infiltrate of lymphocytes, plasma cells, and scattered histiocytes. Microbiological culture and staining was negative. Syphilis serology was negative.

The patient was completely well until 12 months later when he was seen at another hospital with cardiogenic shock. Electrocardiogram showed left bundle-branch block. He had an episode of ventricular tachycardia, and later that day arrested in asystole. All resuscitative measures failed.

Postmortem examination revealed extensive recent infarction of the posterior and lateral left ventricular wall

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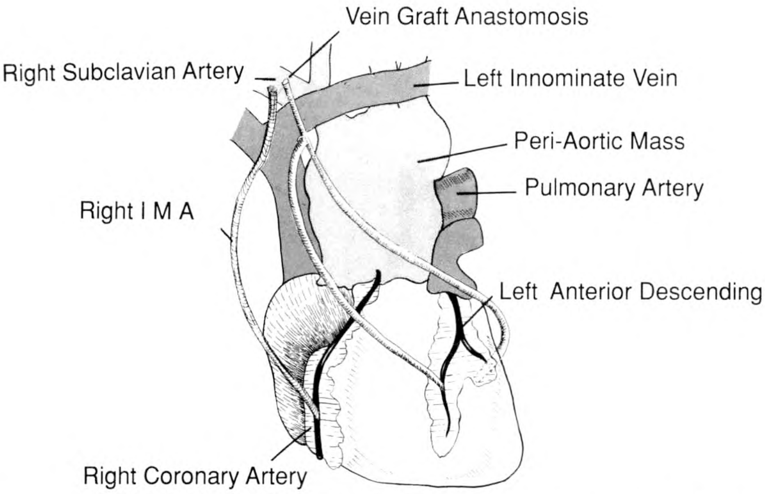

Fig 1. The bypass grafts constructed to overcome the periaortic mass. (IMA = *internal mammary artery.)*

and posterior interventricular septum. The proximal 5 cm of both right and left coronary systems showed severe narrowing, with the walls of the arteries thickened by pale tissue. The grafts were patent and the intima of the aorta, the major aortic branches, and the carotid vessels showed minimal atheroma. Sections of both coronary arteries showed involvement of all layers by the fibroblastic process (Fig 2). The final diagnosis was of fibrosing mediastinitis with coronary artery involvement.

Comment

Fibrosing mediastinitis can be first seen in many ways. It may be an incidental finding of a mass on chest roentgenogram, produce symptoms from compression of mediastinal structures [1], or mimic other clinical conditions such as malignancy, acute inflammatory processes with a lung infiltrate, and recurrent pulmonary thromboembolism [3]. This case demonstrates that angina pectoris due to coronary artery involvement may also occur.

The case described presents the surgeon with several technical problems. Cardiopulmonary bypass was achieved by femoral cannulation. Myocardial preservation is difficult when cross-clamping and cardioplegia cannot be used. A combination of hypothermia and venting of the fibrillating heart has been described [4], and was used in this case. Distal anastomoses were performed with reduced perfusion pressure to improve visibility.

To perform the proximal saphenous vein anastomoses, a number of techniques for the "difficult aorta" have been described [5, 6]. However, these techniques are applicable to the very thick or calcific aorta and would not have been possible in this case. Weinstein and Killen [7] have described the use of the innominate artery, but this vessel was involved by the fibrotic process and thus the anastomosis was placed more distally, on the right subclavian artery. Holland and Hieb [8] have also described the use of the carotid artery origin in 3 patients, together with a mammary graft. The use of the descending thoracic aorta, as described by Hicks [2], is another alternative. The use of a "snake" or sequential graft minimizes the number of proximal anastomoses [6], and in this case a similar effect was achieved by creating a Y-type graft with one proximal

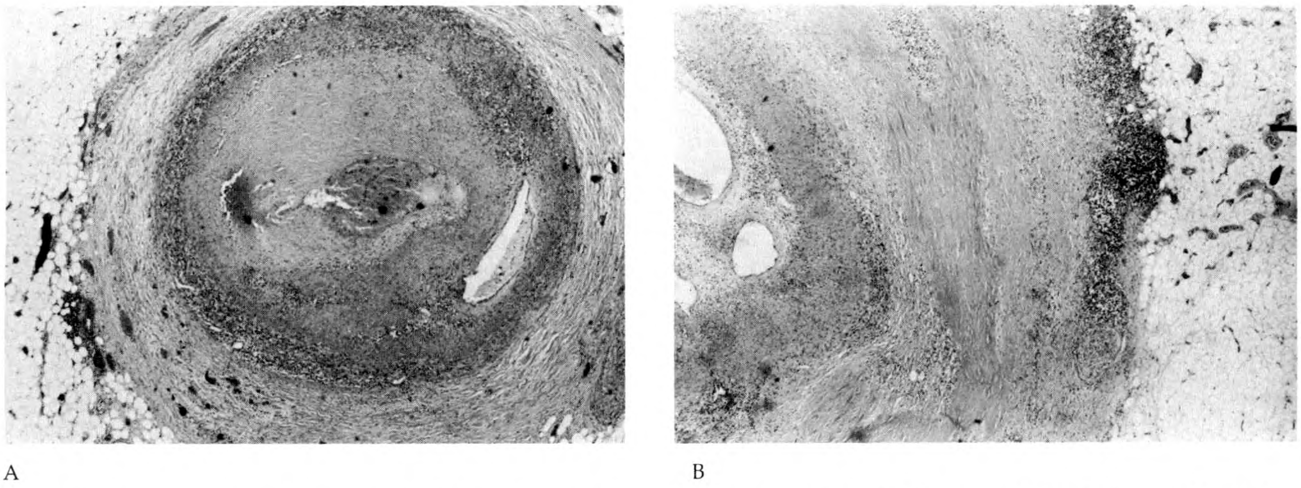

Fig 2. (A) Transverse section of the proximal right coronary artery demonstrating perivascular and inflammatory change in the muscular wall and severe narrowing of the lumen. (Hematoxylin and eosin, ×100 before 52% reduction.) (B) Section of vessel wall and recanalized lumen from the left anterior descending artery demonstrating intimal fibrosis, loss of muscle from the media, inflammatory change, and adventitial fibrosis. (Hematoxylin and eosin, ×250 before 52% reduction.)

anastomosis. Although bilateral mammary grafts could have been used, this technique has been associated with an increased risk of sternal ischemia and infection in diabetic patients and was thus avoided.

Fibrosing mediastinitis is a rare cause of obstruction to major coronary vessels and requires modification of the techniques employed for revascularization and cardiac preservation.

We wish to thank the Pathology Department, Box Hill Hospital, Melbourne, for providing the postmortem pathological slides, and Dr S. Lade, Pathology Department, Alfred Hospital, for his assistance.

References

1. Schowengerdt CG, Suyemoto R, Main FB. Granulomatous and fibrous mediastinitis—a review and analysis of 180 cases. J Thorac Cardiovasc Surg 1969;57:365-79.
2. Hicks GL. Fibrosing mediastinitis complicating coronary artery surgery—use of the descending thoracic aorta. J Cardiovasc Surg 1985;26:514-5.
3. Berry DF, Buccigrossi BS, Peabody J, et al. Pulmonary vascular occlusion and fibrosing mediastinitis. Chest 1986;89:296-301.
4. Akins CW, Carroll DL. Event-free survival following nonemergency myocardial revascularization during hypothermic fibrillatory arrest. Ann Thorac Surg 1987;43:628-33.
5. Ott DA, Cooley DA. The difficult proximal coronary anastomosis. Cardiovasc Dis Bull Tex Heart Inst 1979;6:55.
6. Robicsek F, Rubenstein R. Calcification and thickening of the aortic wall complicating aortocoronary grafting: a technical modification. Ann Thorac Surg 1980;29:84-5.
7. Weinstein G, Killen DA. Innominate artery-coronary artery bypass graft in a patient with calcific aortitis. J Thorac Cardiovasc Surg 1980;79:312-3.
8. Holland DL, Hieb RE. Revascularization without embolization: coronary bypass in the presence of a calcific aorta. Ann Thorac Surg 1985;40:308-10.

REVIEW OF RECENT BOOKS

Lung Cancer Chronicles

By John A. Meyer, MD
New Brunswick, Rutgers University Press, 1989
233 pp, illustrated, $35.00

Reviewed by Benson B. Roe, MD

This concise (233 pages) book provides a readable treatise on a highly important and devastating disease of epidemic proportions that either has already or promises to afflict a large segment of the current adult population. It represents a valuable resource for physicians to provide for their patients who either have or are threatened with this difficult disease.

The author wears each of his three caps with class. As a practicing thoracic surgeon who has a vast experience with this malignancy, he brings the issue into print with the authority of a true expert. As a teacher, he smoothly translates that experience to articulate the essence of the complex technology used to treat the disease. And as a skilled writer, he conveys his message with sufficient interest and empathy to keep the reader engaged. His attractive adjunct to this objective is the introduction to each chapter with one or more pertinent quotations from a wide variety of sources.

The format is simple. A fictitious thoracic surgeon encounters and treats a series of patients, each of whom exemplifies some phase or facet of the disease. He shares with the reader the physician's uncertainties and dilemmas in addressing the clinical findings along with the problems and complications of treatment modalities.

The reader cannot escape the dramatic shadow of cigarette smoking as the clear and undoubted major causative factor. Despite already being well known, this message is so effectively conveyed that it alone makes the book a valuable tool for convincing the skeptics who rationalize their smoking habit or deny its threat. Indeed, it could almost be said that cancer is the secondary theme of a treatise on the effects of smoking.

The comprehensive character of the book is reflected in the chapters that address with clarity and balance the emotional, psychological, economic, and political repercussions of this disease and its principal cause. The author provides a mature perspective to the dubious validity of heroic therapy in the terminal stages of the disease and dwells on the importance of informed choice in the clinical studies to evaluate new chemical agents. Similarly, he provides a dramatic—yet low key—rendition of the enormous power and money in the tobacco industry, their successful thwarting of liability for their lethal product, their leverage in both government and the media, and even the cynical Social Security savings from tobacco-shortened lives.

The dismal character and the magnitude of this disease provide a fertile field for "alternative" (read: quackery) treatments that are hugely remunerative. The broad moral and legal aspects of this issue are viewed in careful balance against the charges of oppression by the "medical monopoly."

For the more intense reader there is an appendix of three chapters on somewhat more esoteric (for the layman) aspects of the disease. These reviews of doubling time mechanics, histological types, and imaging technology are also written with clarity and illustrations that can easily be grasped by the intelligent layman.

Despite my long experience with and considerable knowledge about lung cancer, I found the book to be interesting and informative enough to recommend it not only for my colleagues' patients but also as worthwhile for their own reading.

San Francisco, California

Percutaneous Transaortic Closure of Postinfarctional Ventricular Septal Rupture

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and Chong Yong Shi, MD

Department of Cardiovascular Surgery, The Heart Institute of Japan, Tokyo Womens' Medical College, and Ayase Heart Hospital, Tokyo, Japan

We report a case of successful closure of a postinfarctional ventricular septal defect by means of the transaortic approach with a balloon catheter. This method brought about substantial improvement in cardiopulmonary function before an elective operation and made it possible to successfully perform the operation on the patient, an 81-year-old woman, on the 22nd day of admission.

(Ann Thorac Surg 1991;51:655–7)

Septal rupture is a serious complication of myocardial infarction and has a poor prognosis [1]. We have recently devised a new technique using a balloon catheter to close the transventricular septal shunt, which has proved particularly effective in improving the hemodynamic status (Fig 1). This method was applied to an 81-year-old patient with ventricular septal defect after acute myocardial infarction.

An 81-year-old woman who had had a severe heart attack 20 hours earlier was admitted to our hospital on an emergency basis. On arrival the patient appeared tachypneic, restless, and perspiring. Blood pressure was 100/65 mm Hg, heart rate was 98 beats/min and regular, and central venous pressure was 24 cm H_2O. Assessment revealed bilateral basilar rales and a grade 4/6 high-pitched pansystolic murmur, which was heard best at the left third intercostal space. The electrocardiogram showed a massive myocardial infarction of the broad anterolateral wall (ST elevation was noted in leads V_1 to V_6) and left axis deviation. A chest roentgenogram revealed bilateral pulmonary congestion and heart enlargement. Blood chemistry analyses revealed a serum aspartate aminotransferase level of 325 U/L and a creatine kinase level of 1,905 U/L.

Aggressive medical management temporarily resulted in clinical improvement. However, on the second day of admission, intraaortic balloon pumping was started to assist the cardiac function. Although surgical intervention was indicated, it was rejected by the patient and her family. On the ninth day, coronary angiography was performed and revealed complete occlusion of the proximal left anterior descending artery and severe coronary stenosis of the left circumflex artery (95%) and right coronary artery (99%). Left ventriculography revealed a left ventricular aneurysm and a left-to-right shunt with a shunt ratio of 0.65. Ejection fraction of the left ventricle was 0.41. When coronary angiography was instituted, the heart arrested and cardiac resuscitation with cardiac massage and intratracheal intubation was urgently performed. After the examination, the hemodynamic status further deteriorated. Pulmonary artery pressure was increased to 55 mm Hg, and urine volume was seriously decreased owing to low cardiac output syndrome.

On the 18th day, because the hemodynamic status had extremely deteriorated, a balloon catheter (model 93A-119-7F; American Edwards Laboratories, Irvine, CA) was inserted under radiographic guidance from the femoral artery to the left ventricle. Subsequently, the balloon was inflated with 1 mL of air to enable it to pass through the defect with the bloodstream, and it was thus successfully introduced into the right ventricle. Pressure was monitored at the end of the catheter. When the pressure monitor indicated that the catheter was situated in the right ventricle, the balloon was then inflated with 3 mL of air, so that the balloon size was approximately 20 mm in diameter, and drawn against the interseptal wall to close the defect. Angiography was performed from the proximal hole of the catheter and revealed complete closure of the left-to-right shunt (Fig 2). The shunt ratio was substantially decreased from 0.64 before the procedure to 0.10 after the closure. The balloon catheter was secured at the point of insertion with a stay stitch. The hemodynamic status dramatically improved after this procedure: pulmonary artery pressure was reduced from 51/15 to 39/13 mm Hg.

The patient underwent an operation on the 22nd day after the first admission. Once cardiopulmonary bypass was instituted, coronary artery bypass was sequentially performed to the right coronary artery and to the left circumflex artery using a saphenous vein graft. Through incision of the aneurysm, the ventricular septal defect, which measured 15 × 17 mm, was exposed. The defect was located on the anterior ventricular septum and penetrated to the outflow tract of the right ventricle. It was closed with a Dacron patch (20 × 15 mm) using ten interrupted mattress sutures. Aneurysmal tissue of the left ventricle was resected, and the incision was closed by

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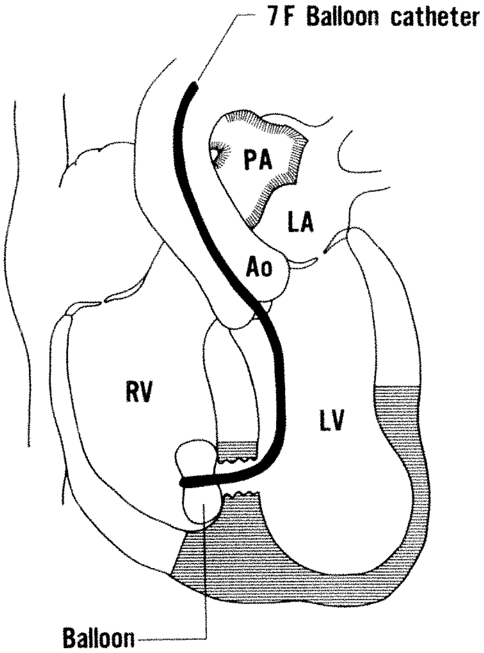

Fig 1. Technique used in occluding the ventricular septal defect with the balloon catheter. (Ao = *aorta;* LA = *left atrium;* LV = *left ventricle;* PA = *pulmonary artery;* RV = *right ventricle.)*

reinforcing the Teflon patch. The postoperative course of this patient was uneventful and she was discharged from the hospital.

Comment

The natural history of this serious complication after acute myocardial infarction is an extremely poor outlook, and 91% of the patients die within 1 month after the onset [2]. Heltmiller and associates [3] reported 25% hospital mortality in patients operated on early. Kitamura and coworkers suggested that operative intervention should be delayed until 6 to 8 weeks after infarction, because healing after myocardial infarction was not remarkable until after the third week [4]. The mortality rate in cases where operation was performed after 3 weeks was 5%. Because the high early mortality in patients with this lesion rarely permits such a delay, intervention that stabilizes hemodynamic status in the acute phase might be useful to improve the surgical result [5].

Babb and associates [6] decreased the shunt by increasing right ventricular afterload by obstructing the outflow of the right ventricle with a balloon catheter. This procedure decreased the amount of left-to-right shunting in the experimental model. However, this approach may induce right ventricular failure and is particularly inadequate in patients with inferior wall infarction. More recently, Colton and associates [7] designed a balloon catheter to close a ventricular septal defect. Prototype devices were fabricated with two disk-shaped balloons mounted on a multiple-lumen angioplasty catheter and experimentally tested. These results indicated the efficacy of the device and its potential for clinical use. These previous studies were all animal experiments.

Recent technical advances using newer prosthetic materials and preoperative pharmacological management also have led to favorable early operative results. Skillington and colleagues [8] reported that the overall early mortality rate was 20.8%, although their most recent experience with 36 patients (January 1987 to October 1988) showed a decline to 11.1%. However, Radford and associates [9] suggested that patients with cardiogenic shock and multiorgan failure due to low output syndrome have poor results after early operation. In the present case, a poor expectation of operation was indicated as the patient

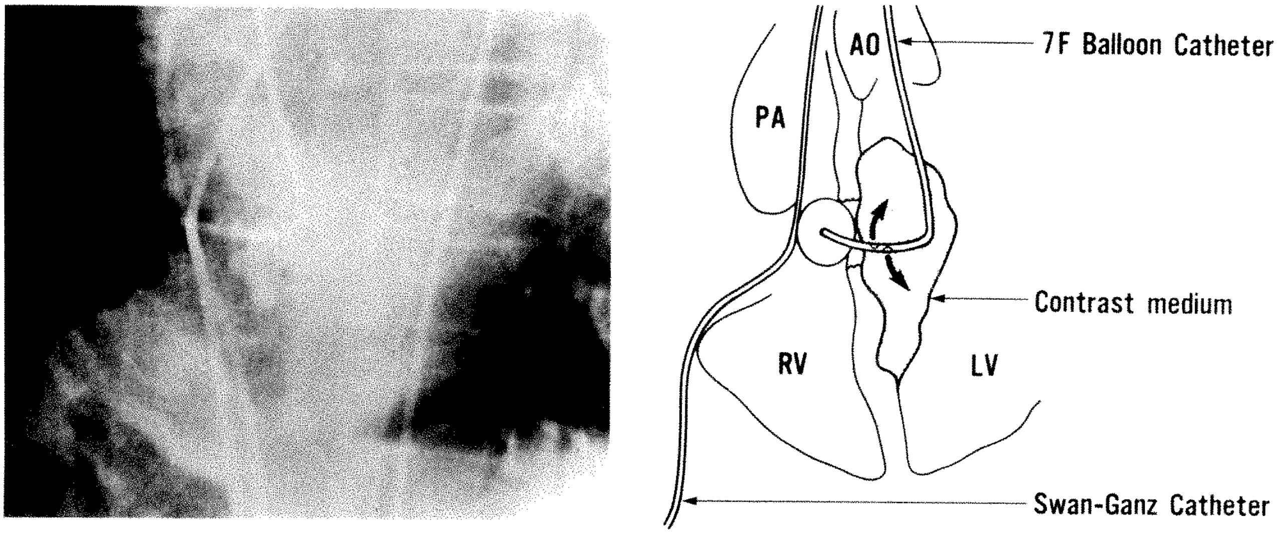

Fig 2. Angiogram showing the catheter passed through the defect. The balloon was inflated with 3 mL of air, and it plugged the interventricular defect. Angiography was performed through the hole placed in the left ventricle. The left-to-right shunt was completely sealed with the balloon. (AO = *aorta;* LV = *left ventricle;* PA = *pulmonary artery;* RV = *right ventricle.)*

was 81 years old, had associated cardiogenic shock, and showed subsequent hemodynamic deterioration. Pulmonary congestion was progressive from the tenth day. Intraaortic balloon pumping was no longer supportive on the 18th day. Therefore, we applied the new technique using a balloon catheter, which occluded the defect and reduced the left-to-right shunt to improve the clinical course. With this procedure, the shunt ratio was decreased and the hemodynamic status was improved. The operation was successfully performed on the 22nd day after the onset of myocardial infarction.

In conclusion, a new procedure using a balloon technique was useful in closing the ventricular septal defect and reducing the shunt. It was shown to be not only effective in improving the hemodynamic status of the patient, but also useful for delaying the operation to a safe period after the occurrence of a ventricular septal defect.

References

1. Oyamada A, Queen FB. Spontaneous rupture of the interventricular septum following acute myocardial infarction with some clinicopathological observations on survival in five cases. Presented at the Pan Pacific Pathology Congress, Tripler US Army Hospital, Honolulu, HI, Oct 12, 1961.
2. Sanders RJ, Kern WH, Blount SG. Perforation of the interventricular septum complicating myocardial infarction. Am Heart J 1956;51:736–48.
3. Heitmiller R, Jacobs ML, Daggett WM. Surgical management of postinfarction ventricular septal rupture. Ann Thorac Surg 1986;41:683–91.
4. Kitamura S, Mendez A, Kay JH. Ventricular septal defect following myocardial infarction: experience with surgical repair through a left ventriculotomy and review of literature. J Thorac Cardiovasc Surg 1971;61:186–99.
5. Brandt B, Wright CB, Ehrenhaft JL. Ventricular septal defect following myocardial infarction. Ann Thorac Surg 1979;27:580–9.
6. Babb JD, Waldhausen JA, Zelis R. Balloon-induced right ventricular outflow obstruction: a new approach to control of acute interventricular shunting after myocardial infarction in canines and swine. Circ Res 1977;40:372–9.
7. Colton JS, Hynds EJ, Churchwell AL. Balloon catheter closure of postinfarction ventricular septal defects. Bioengineering 1988;8:11–4.
8. Skillington PD, Davies RH, Luff AJ, et al. Surgical treatment for infarct-related ventricular septal defects. J Thorac Cardiovasc Surg 1990;99:798–808.
9. Radford MJ, Johnson RA, Daggett WM, et al. Ventricular septal rupture: a review of clinical and physiologic features and an analysis of survival. Circulation 1981;64:545–51.

Pulmonary Artery Balloon Counterpulsation for Intraoperative Right Ventricular Failure

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Two cases of severe low cardiac output and right ventricular failure after coronary artery bypass grafting necessitated pulmonary artery balloon counterpulsation after intraaortic balloon pumping and maximal inotropic/pressor support were unsuccessful in maintaining a satisfactory cardiac output. Hemodynamic improvement was sufficient to allow removal of the device 2 and 3 days postoperatively, with survival in 1 patient. Pulmonary artery counterpulsation is less morbid in comparison with other mechanical methods of right ventricular support and is applicable in right ventricular failure of intermediate severity.

(Ann Thorac Surg 1991;51:658–60)

Successful use of pulmonary artery balloon counterpulsation (PABC) with ultimate patient survival has been described for intraoperative right ventricular (RV) failure in association with pulmonary hypertension [1, 2]. Right ventricular pump failure occurring with normal pulmonary artery pressure may also preclude weaning from cardiopulmonary bypass (CPB). Usually this occurs in the setting of biventricular failure after adequate treatment of the left heart component either by intraaortic balloon pumping or with a left ventricular assist device. In this paper we report PABC in 2 patients who suffered severe RV failure after a coronary bypass operation. This supportive measure was initiated after traditional methods of intraaortic balloon counterpulsation and maximal pharmacological support had been exhausted.

Case Reports

Patient 1

A 73-year-old man underwent reoperation coronary artery bypass grafting with a left internal mammary artery to the left anterior descending artery and a saphenous vein to the obtuse marginal branch of the circumflex artery. A small, occluded posterior descending coronary artery was not grafted. After 19 minutes of aortic cross-clamping the patient was initially weaned satisfactorily from CPB without inotropes. However, a progressive decrease in blood pressure and cardiac output necessitated an epinephrine infusion and the intraaortic balloon pump was inserted. Cardiac output was still inadequate. The sternum was reopened and CPB was rapidly reestablished. Both grafts appeared patent, although there was concern that the left internal mammary artery flow was insufficient or that ischemia in the territory of the ungrafted right coronary artery may have contributed to the cardiovascular collapse. Consequently, two vein grafts to the left anterior descending artery and posterior descending coronary artery were constructed during an additional 20 minutes of aortic clamping and cold cardioplegic arrest.

Right heart failure occurred on weaning from CPB, as evidenced by a dilated, poorly contractile appearance and the following pressures: right atrial, 25 mm Hg; left atrial, 8 mm Hg; pulmonary artery pressure, 38/20 mm Hg, and mean arterial pressure, 50 mm Hg. The patient was unable to be separated from bypass despite maximal catecholamine support, intraaortic balloon pumping, and prostaglandin E_1.

Pulmonary artery balloon counterpulsation was initiated while the patient was on full CPB. A low-porosity Dacron tube graft (18 mm × 30 cm) was anastomosed end-to-side to the main pulmonary artery with 4-0 Prolene suture. A 40-mL balloon was positioned inside the graft (Fig 1). Hemostasis was secured by tying an umbilical tape tightly around the Dacron graft just beyond the balloon. The sternotomy was not closed, and an elliptical sterile rubber dressing was used to cover the heart, Dacron graft, and its contained balloon pump.

Right ventricular systolic function noticeably improved and the patient was weaned off CPB easily. The patient remained in stable condition in the intensive care unit with a mean arterial pressure of 70 to 80 mm Hg, left atrial and right atrial pressures of 12 to 14 mm Hg, and a cardiac index greater than 1.8 $L \cdot min^{-1} \cdot m^{-2}$. Pulmonary artery pressure was 38/18 mm Hg.

To minimize thrombus formation around the balloon, a continuous intravenous infusion of dextran 40 was run at 20 mL/h, after chest tube drainage had decreased to less than 50 mL/h for 2 consecutive hours. Perioperative myocardial infarction was ruled out. The patient was returned to the operating room for removal of the balloon 60 hours postoperatively, after demonstrating a satisfactory cardiac index (>2.0 $L \cdot min^{-1} \cdot m^{-2}$) with the balloon

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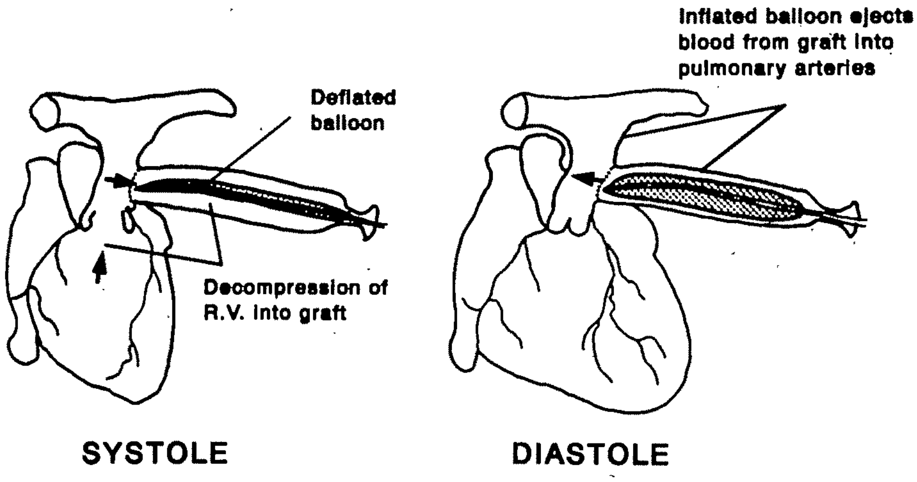
Inflated balloon ejects blood from graft into pulmonary arteries
Deflated balloon
Decompression of R.V. into graft
SYSTOLE
DIASTOLE

Fig 1. Dacron graft containing pulmonary artery balloon counterpulsation device in situ. (R.V. = *right ventricle.)*

weaned to 1:3. The balloon was removed, the graft was clamped and divided 3 to 4 cm above the pulmonary artery, and the end was oversewn. He recuperated without further complication and was discharged on the 20th postoperative day. Eight months later, he is in New York Heart Association class I, on 1 aspirin tablet per day.

Patient 2

A 69-year-old woman underwent routine coronary artery bypass grafting using a left internal mammary artery graft to the left anterior descending artery and a saphenous vein graft to the obtuse marginal branch. The operation was uneventful, and the patient had stable hemodynamics after bypass. however, 1 hour after return to the intensive care unit, ventricular fibrillation suddenly developed, which proved refractory to direct-current cardioversion and antiarrhythmic therapy. She was returned to the operating room, cardiac output being maintained with closed chest massage, and then placed back on CPB support. The reason for this sudden deterioration was unclear although the left internal mammary artery was small and possibly in spasm. Two additional saphenous vein grafts were constructed, an additional left anterior descending artery graft and one to the right coronary artery for possible undiagnosed right coronary artery ostial stenosis. Cardiopulmonary bypass was unable to be discontinued despite intraaortic balloon pumping and maximum inotropic support. A diagnosis of RV failure was made by the same criteria as in the previous case and PABC was established using a similar method.

Right ventricular contractile function was visibly improved, and the cardiac chamber pressures were as follows: mean arterial pressure, 85 mm Hg; right atrial pressure, 10 mm Hg; left atrial pressure, 4 mm Hg, and pulmonary artery pressure, 32/16 mm Hg; the cardiac index was 2.1 $L \cdot min^{-1} \cdot m^{-2}$.

After transfer to the intensive care unit, return trips to the operating room were required at 24 hours for main pulmonary artery–Dacron graft anastomotic hemorrhage and at 48 hours because of balloon malfunction due to kinking of the concealed cable. Because the patient was stable without its support, the PABC was removed. The patient then remained stable for 24 hours before low cardiac output developed with oliguric renal failure and required increasing inotropic support. Further deterioration occurred and the patient died 5 days postoperatively.

Comment

Experimental studies by Kralios [3], Spotnitz [4], and their associates in the early 1970s showed that PABC could improve hemodynamic function in RV failure. Subsequently, Spence, Jett, and others [5–10] reported that RV failure created by increased pulmonary vascular resistance or by diminished RV pump function could be ameliorated with PABC. Patient survival with PABC has not been documented in postbypass RV failure associated with normal pulmonary artery pressures, although there have been reported cases in which weaning from CPB was made possible in this situation [2, 11].

The cause of RV failure in both these cases is speculative, although biventricular dysfunction was almost certainly present and PABC appeared to adequately treat the RV component.

The appropriate assist device for RV failure that is severe enough to limit weaning from CPB despite intraaortic balloon pumping and maximal pharmacological support is either PABC or right ventricular assist devices. Spence and associates [6] have suggested that when RV output is depressed by less than 50% from baseline, PABC will be effective in restoring acceptable hemodynamics. We concur with that and suggest PABC as a less morbid method especially suited for use in moderate RV failure avoiding the advanced forms of ventricular assist with their attendant complex logistics. Whereas right ventricular assist devices may not be a uniformly applicable form of support, PABC should be part of the armamentarium of all cardiac surgical units.

References

1. Flege JB, Wright CB, Resinger TJ. Successful balloon counterpulsation for right ventricular failure. Ann Thorac Surg 1984;37:167–8.
2. Symbas PN, McKeown PP, Santora AH, Vlasis SE. Pulmonary artery balloon counterpulsation for treatment of intra-

operative right ventricular failure. Ann Thorac Surg 1985;39: 437–40.
3. Kralios AC, Zwart HHJ, Moulopoulos SD, et al. Intrapulmonary artery balloon pumping. J Thorac Cardiovasc Surg 1970;60:125–32.
4. Spotnitz HM, Berman MA, Reis RL, et al. The effects of synchronized counterpulsation of the pulmonary artery on right ventricular hemodynamics. J Thorac Cardiovasc Surg 1971;61:167–74.
5. Spence PA, Peniston CM, Salerno TA, et al. A rational approach to the selection of an assist device for the failing right ventricle. Ann Thorac Surg 1986;41:606–8.
6. Spence PA, Weisel RD, Salerno TA, et al. The hemodynamic effects and mechanism of action of pulmonary artery balloon counterpulsation in the treatment of right ventricular failure during left heart bypass. Ann Thorac Surg 1985;39:329–35.
7. Jett GK, Siwek LG, Picone AL, et al. Pulmonary artery balloon counterpulsation for right ventricular failure. J Thorac Cardiovasc Surg 1983;86:364–72.
8. Jett GK, Picone AL, Clark RE. Circulatory support for right ventricular dysfunction. J Thorac Cardiovasc Surg 1987;94: 95–103.
9. Spence PA, Weisel RD, Salerno TA, et al. Pulmonary artery balloon counterpulsation in the management of right heart failure during left heart bypass. J Thorac Cardiovasc Surg 1985;89:264–8.
10. Miller DC, Moreno-Cabral RJ, Stinson EB et al. Pulmonary artery balloon counterpulsation for acute right ventricular failure. J Thorac Cardiovasc Surg 1980;80:760–3.
11. Dreyfus A, Guilleman R, Carpentier A. Assistance ventriculaire droite par contrepulsion intrapulmonaire. Arch Mal Coeur 1989;82:81–6.

The European Association for Cardio-Thoracic Surgery Notice of Annual Meeting

The Fifth Annual Meeting of the European Association for Cardio-Thoracic Surgery will be held September 22-25, 1991, at the Royal Lancaster Hotel in London, United Kingdom. The scientific sessions are open to all registered participants. The registration fee includes admission to the entire scientific program, meeting documentation, welcome reception on Sunday evening, concert on Monday evening, and tea and coffee.

Registration and Hotel Reservation

All participants of the meeting should request a registration form from Conference Associates & Services Ltd, EACTS, Congress House, 55 New Cavendish St, London W1M 7RE, United Kingdom (telephone: 071 486 0531; facsimile: 071 935 7559).

Intrapericardial Pheochromocytoma

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In a 34-year-old man with hypertension and increased urinary catecholamine excretion for 12 years, an *m*-[^{131}I]iodobenzylguanidine scan and chest computed tomography located an intrapericardial pheochromocytoma in the left atrium. The tumor was excised through a left thoracotomy with cardiopulmonary bypass and circulatory arrest. At 34-month follow-up, blood pressure and urine catecholamine levels were normal. In the 15 cases of intrapericardial pheochromocytoma treated by resection reported in the literature, all 11 survivors were symptom-free except 1 who had residual left atrial tumor and multiple skeletal metastatic lesions. Computed tomography directed by the *m*-[^{131}I]iodobenzylguanidine scan can be used for detailed location of the tumor. Appropriate surgical approach and use of cardiopulmonary bypass are critical in the resection of these highly vascular tumors.

(Ann Thorac Surg 1991;51:661–3)

Pheochromocytomas are catecholamine-secreting tumors that arise principally from cells of the autonomic nervous system. Fewer than 2% of these tumors develop within the thorax, and the majority of intrathoracic pheochromocytomas are in the posterior mediastinum [1]. Tumors within the pericardium are extremely rare. To date, only 15 attempts at excision of intrapericardial pheochromocytomas have been reported [2–13].

We describe a patient who had a history of hypertension of 12 years' duration and was subsequently found to have a dopamine- and norepinephrine-secreting pheochromocytoma arising from the left atrium and left pulmonary vein.

A 34-year-old man who had had hypertension, diaphoresis, palpitations, facial flushing, and increased urinary catecholamine excretion for 12 years was admitted with right hemiparesis due to left putaminal hemorrhage. Pheochromocytoma had been suspected previously but could not be located. However, a second *m*-[^{131}I]iodobenzylguanidine (MIBG) scan showed focal areas of increased uptake in the thorax just left of the midline (Fig 1A). Subsequent chest computed tomography confirmed a lobulated, heterogeneously enhanced mass in the subcarinal and left hilar areas, between the left atrium and left pulmonary vein and artery (Fig 1B). An extraadrenal, intrapericardial pheochromocytoma was suspected, and surgical resection of the tumor was undertaken.

The thoracic cavity was entered through a left posterolateral thoracotomy in the fourth intercostal space. At pericardiotomy, a 6 × 4 × 3-cm, lobulated, highly vascular tumor was found on the posterior wall of the left atrium and extending to the left pulmonary vein and carina.

The left atrium was opened at the junction with the left pulmonary vein, and the tumor was completely removed along with a patch of left atrium and left pulmonary vein. Bovine pericardium was used to repair the atrial wall defect. Cardiopulmonary bypass was reestablished and the patient was removed from circulatory support without incident.

The patient had an uneventful postoperative recovery and was normotensive without medication. Follow-up chest computed tomography 8 months postoperatively demonstrated no new tumor growth. Thirty-four months later, urine and serum catecholamine values were within the normal range, and the patient continued to be free of symptoms.

Comment

Pheochromocytoma is a potentially fatal, but resectable, catecholamine-secreting tumor. Intrapericardial pheochromocytomas are extremely rare.

As in our case, the catecholamines produced by all previously reported pericardial lesions were predominately norepinephrine, which is characteristic of extraadrenal pheochromocytomas. This should assist in localization because epinephrine-secreting pheochromocytomas are almost uniformly located at the adrenal glands. However, as in the patient reported by Awoke and Perlstein [2], the dopamine level was increased in our patient.

The clinical picture and biochemical data can suggest the diagnosis of pheochromocytoma, but localization of extraadrenal lesions can be challenging. MIBG scintigraphy has helped tremendously in localizing extraadrenal catecholamine-producing tumors, particularly those in the middle mediastinum [8]. This technique allows scanning of the entire body for tumor and distant metastasis. For catecholamine-secreting tumors in general, a sensitivity of up to 85% and a specificity of up to 96% were reported [14]. The first MIBG scan of our patient did not

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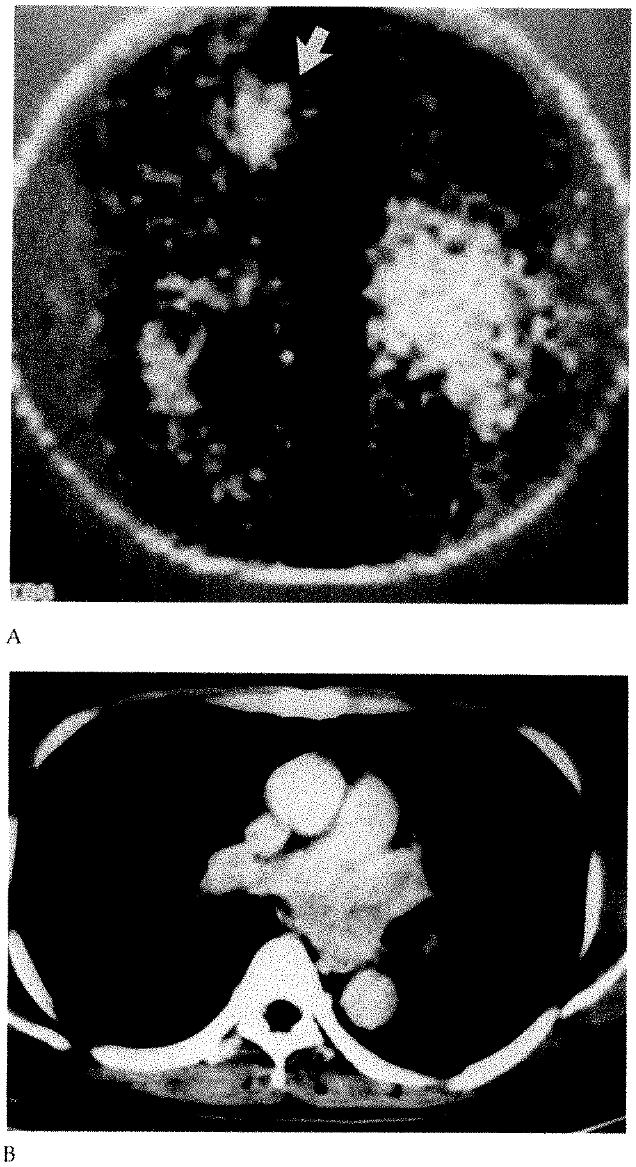

Fig 1. Localization of the tumor. (A) Posteroanterior view of MIBG scan, showing a focal area of increased uptake in the chest cavity, left of the midline (arrow). *(B) Computed tomographic scan of the chest at the level of the subcarinal area shows lobulated, heterogeneous enhanced mass in the subcarinal and left hilar areas.*

detect the tumor. However, a second MIBG scan was positive, demonstrating that repeated MIBG scans are warranted and may reveal a previously undetected pheochromocytoma. Although the exact anatomical location cannot be ascertained from the MIBG scintigraphic studies, such studies can direct subsequent computed tomography to the area of interest [14]. Indeed, there were 15 MIBG scans performed in 12 cases of pheochromocytoma, and 12 were positive. Computed tomography demonstrated pheochromocytoma in 11 of 16 scans; magnetic resonance imaging was performed in 1 case and also revealed the tumor [11]. Magnetic resonance imaging is well suited for evaluating the extent of intracardiac tumor invasion because of the natural contrast among flowing blood, myocardium, and tumor tissue and because of the easy orientation of the plane of section. Indeed, if available, it could be the preferred imaging tool.

Intrapericardial pheochromocytomas usually are located on the posterior wall of the left atrium but can occur in other locations in the heart. Twelve of the 16 resected tumors were located on the atria and 4 involved the ventricle.

For adequate surgical management, it is essential to define the origin of the blood supply to the tumor. Because many intrapericardial tumors have a substantial component of their arterial supply coming from the coronary arteries, coronary arteriography should be performed routinely. The best operative approach is determined by where in the heart the tumor is located. Tumors arising from the posterior left atrial wall near the right pulmonary vein or artery are best approached through a right thoracotomy. Tumors on the right atrium, interatrial groove, or ventricular surface are best approached through a median sternotomy. Tumors originating from the posterior aspect of the left atrium near the left pulmonary veins, as in our case, can be resected through a left thoracotomy to optimize exposure and hemostasis. Indeed, in the only other reported case of a pheochromocytoma in this location, the right thoracotomy approach made exposure and hemostasis difficult, and the patient eventually died of uncontrollable hemorrhage [5].

In planning the operation it also is important to recognize that cardiac pheochromocytomas are not well encapsulated and can be tightly adherent to or infiltrated into the wall of the atrium or ventricle. Indeed, surgical excision should not be undertaken with the expectation that the tumor simply can be "shelled out" [7]. As in our case, adequate resection usually necessitates full-thickness excision of the tumor-containing portion of the atrial or ventricular wall with pericardial replacement.

Another consideration is routine preoperative administration of α- and β-adrenergic blockers to prevent the intraoperative hypertension and arrhythmias that can occur during manipulation of these catecholamine-secreting tumors. However, the only definitive way to prevent these potentially catastrophic complications is to use cardiopulmonary bypass to isolate the heart from the systemic circulation [5].

Surgical cure of cardiac pheochromocytoma was achieved in all survivors of complete surgical excision of the tumor. When the tumor was only partially resected because of extensive myocardial infiltration, survival was symptom-free [7] if metastasis had not occurred [8]. However, when only tumor biopsy and palliative coronary artery bypass grafting are done, symptoms soon recur [11].

References

1. Benjamin SP, McCormack LJ, Effler DB, Groves LK. Primary tumors of the mediastinum. Chest 1972;62:297–303.
2. Awoke S, Perlstein RS. Dopamine- and norepinephrine-secreting intrapericardial pheochromocytoma in a normotensive patient. South Med J 1985;78:994–8.

3. Dunn GD, Brown MJ, Sapsford RN, et al. Functioning middle mediastinal paraganglioma (phaeochromocytoma) associated with intercarotid paragangliomas. Lancet 1986;1:1061–4.
4. Besterman E, Bromley LL, Peart WS. An intrapericardial phaeochromocytoma. Br Heart J 1974;36:318–20.
5. Orringer MB, Sisson JC, Glazer G, et al. Surgical treatment of cardiac pheochromocytomas. J Thorac Cardiovasc Surg 1985;89:753–7.
6. Gross JL, Azevedo MJ, Ludwig EB, de los Santos A, Pinto JF. Cardiac pheochromocytoma [Letter]. Am J Med 1987;83:1013.
7. Saad MF, Frazier OH, Hickey RC, Samaan NA. Intrapericardial pheochromocytoma. Am J Med 1983;75:371–6.
8. Shapiro B, Sisson J, Kalff V, et al. The location of middle mediastinal pheochromocytomas. J Thorac Cardiovasc Surg 1984;87:814–20.
9. Cooley DA, Reardon MJ, Frazier OH, Angelini P. Human cardiac explantation and autotransplantation: application in a patient with a large cardiac pheochromocytoma. Tex Heart Inst J 1985;12:171–6.
10. David TE, Lenkei SC, Marquez-Julio A, Goldberg JA, Meldrum DAN. Pheochromocytoma of the heart. Ann Thorac Surg 1986;41:98–100.
11. Stowers SA, Gilmore P, Stirling M, et al. Cardiac pheochromocytoma involving the left main coronary artery presenting with exertional angina. Am Heart J 1987;114:423–7.
12. Shimoyama Y, Kawada K, Imamura H. A functioning intrapericardial paraganglioma (pheochromocytoma). Br Heart J 1987;57:380–3.
13. Wilson AC, Bennett RC, Niall JF, Clarebrough JK, Doyle AE, Louis WJ. An unusual case of intrathoracic phaeochromocytoma. Aust N Z J Surg 1974;44:27–32.
14. Swensen SJ, Brown ML, Sheps SG, et al. Use of ^{131}I-MIBG scintigraphy in the evaluation of suspected pheochromocytoma. Mayo Clin Proc 1985;60:299–304.

REVIEW OF RECENT BOOKS

Pleural Diseases, Second Edition
By Richard W. Light, MD
Philadelphia, Lea & Febiger, 1990
331 pp, illustrated, $57.50

Reviewed by Richard G. Fosburg, MD

This single-author text comes close to an encyclopedic discussion of pleural disease and reflects the author's long-standing interest in the topic. The first edition of 1983 was intended as a reference text for the practicing physician. This edition reflects the advancing knowledge of the intervening years. The author reviewed more than 500 articles to bring the reader new perspectives including modified theories on the mechanisms for formation and reabsorption of pleural fluid.

The first three chapters review the anatomy, physiology, and radiography of the pleura. Chapter 4 deals with clinical manifestations and useful tests. The use of immunohistochemical tests with monoclonal antibodies and flow cytometry are included. Other new diagnostic tests include pleural fluid antinuclear antibody (lupus pleuritis), pleural fluid adenosine deaminase, lysozyme, and γ-interferon levels (tuberculous pleuritis). Chapter 5 presents algorithms for separation of transudates from exudates, for evaluating the appearance of pleural fluid, and for evaluating patients with normal or low glucose levels. The next 13 chapters deal with etiology. Chapters 19, 20, and 21 deal with pneumothorax, hemothorax, and chylothorax, respectively. The twenty-second chapter addresses pleural calcification, asbestos, fibrothorax, and intrathoracic splenosis. The last two chapters discuss the procedures of thoracentesis, pleural biopsy, and chest tubes.

Each chapter has its references up to 1989. The radiographs, tables, and illustrations are well done. The text is very readable. Those chapters dealing with specific etiologies are neither definitive nor too abbreviated. Most issues are quite thoroughly detailed and appropriate for this particular type of volume. It will be a useful addition to the libraries of all those interested in thoracic diseases.

La Jolla, California

Spontaneous Late Rupture of an Aortocoronary Saphenous Vein Graft

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A case is presented of vein graft rupture leading to myocardial infarction and subsequent pseudoaneurysm formation.

(Ann Thorac Surg 1991;51:664–6)

The late complications of aortocoronary artery–saphenous vein bypass grafting include stricture at the anastomotic site, occlusion of the graft by atheromatous plaques, fibrous intimal hyperplasia of the graft [1], coronary steal syndrome, disruption of the proximal anastomosis, and aneurysm formation at any cannulation site. Aneurysmal dilatation of the vein graft is rare [2, 3], and rupture of the body of the graft is very unusual [4, 5]. We present a case of late rupture of the body of an aortocoronary artery–saphenous vein bypass graft with subsequent pseudoaneurysm formation.

A 63-year-old man with a medical history of atherosclerotic coronary artery disease and peripheral vascular disease was admitted for coronary artery bypass reoperation because of unstable angina. In 1977 the patient underwent uncomplicated triple aortocoronary artery–saphenous vein bypass grafting. He remained asymptomatic until 3 years before admission, when he again experienced chest pain. He then suffered a myocardial infarction. Chest roentgenogram (Fig 1) showed an additional density in the region of the left hilum. Because of postinfarction angina, cardiac catheterization was done. This revealed a 50% occlusion of the left main coronary artery and a clinically significant lesion of the left anterior descending artery. All bypass grafts were occluded. Of note was a short aneurysmal stump of vein graft (Fig 2). Computed tomographic scan of the chest with contrast medium (Fig 3) showed a large mediastinal mass to the left of the main pulmonary artery descending to the base of the heart and down into the atrioventricular groove. A small portion of this mass opacified, indicating that it was of vascular origin. A thoracic aortogram was performed to determine the site of origin of the aneurysm. A small area of double density was seen in the ascending aorta.

His operation was done 4 months after his infarct. The patient was placed on hypothermic cardiopulmonary bypass. A short stump of the saphenous vein graft proximal to a pseudoaneurysm was ligated. The mediastinal mass was found to be secondary to a ruptured vein graft. The neck of the pseudoaneurysm involved 35% of the free wall of the saphenous vein graft just beyond the proximal anastomosis. Organized clot and free blood was seen to travel over the pulmonary artery and down into the posterior atrioventricular groove just beyond the left atrial appendage, clearly molded by the heart structures and pericardium. Interestingly, the distal portion of the graft was also patent (Fig 4). Double coronary artery bypass was then performed with saphenous vein and left internal mammary artery grafts. The patient was easily taken off bypass on low dose inotropic support. The remainder of the hospital course was uneventful.

Pathologic evaluation of the remaining portion of sa-

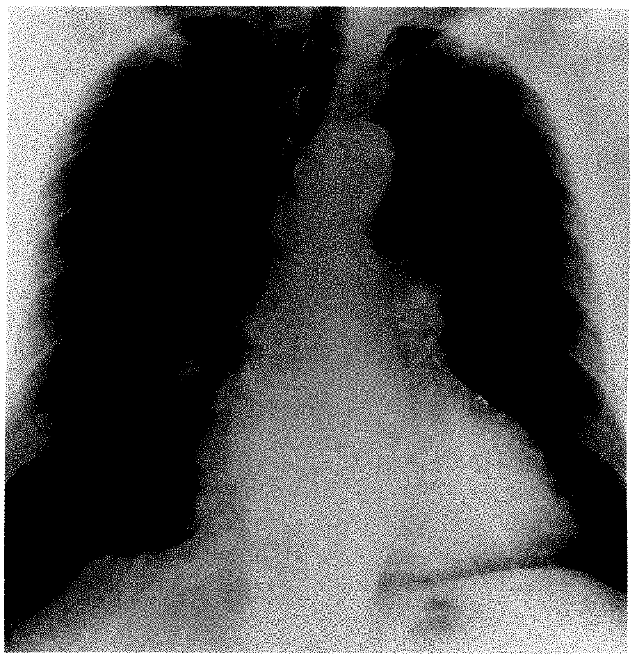

Fig 1. Chest roentgenogram showing left hilar mass.

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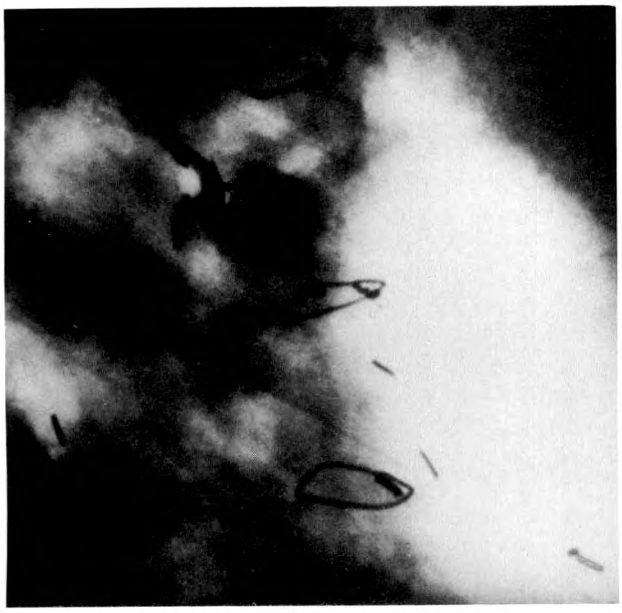

Fig 2. Cardiac catheterization revealing pseudoaneurysm of proximal vein graft.

phenous vein at the site of rupture showed an adherent thrombus (0.9 cm in diameter) sitting in the vascular channel. There were marked changes of the intima consisting of fibrous and secondary hyalinization. The media and adventitia were both congested.

Comment

Aneurysmal dilatation of the body of an aortocoronary saphenous vein graft is a rare complication of bypass grafting [2, 3]. This may be the result of atheromatous or nonatheromatous processes. Early aneurysm formation occurring at 4 and 6 months postoperatively has been found to be the result of preexisting unrecognized vein wall weakness or injury at the time of harvest [2]. Vlodaver and Edwards [1] found that aneurysms of vein grafts in place for 3½ months or longer consistently showed either organized thrombi or intimal fibrotic proliferation. Aneurysms discovered between 5 and 9 years postoperatively were all atherosclerotic in nature [3, 5]. Late rupture of a vein graft aneurysm has only been reported in recent literature. The sequelae of this can include free rupture into the thoracic cavity, producing an acute hemothorax [4], and contained rupture with pseudoaneurysm formation and myocardial infarction [5].

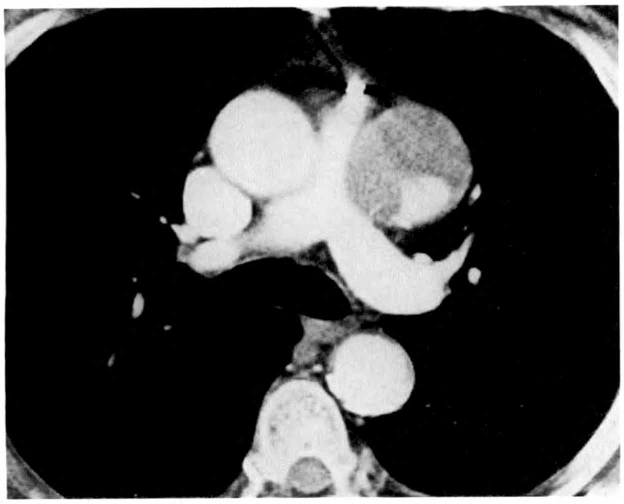

Fig 3. Computed tomographic scan revealing left hilar mass (see text).

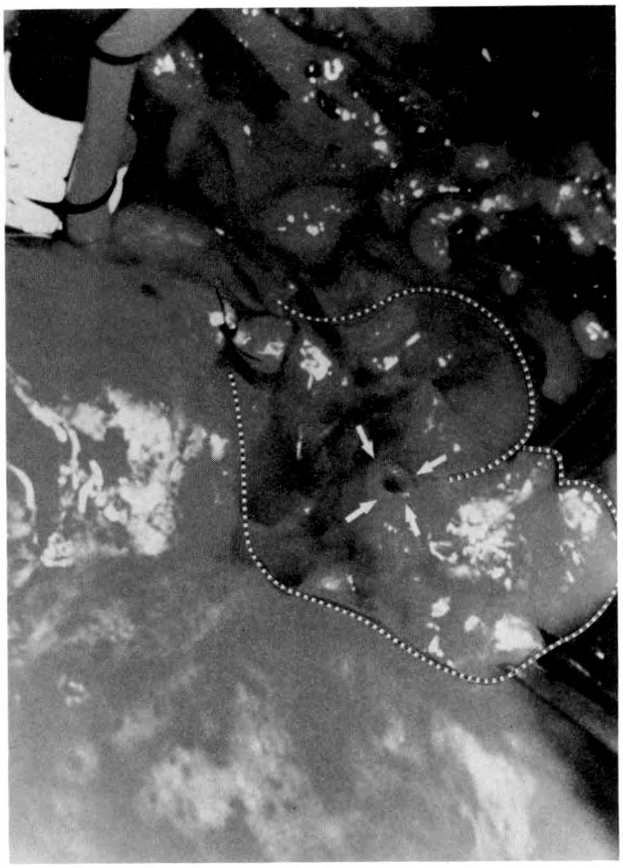

Fig 4. Intraoperative photograph (from patient's right) revealing ligated proximal vein graft, open distal vein graft, and local extent of pseudoaneurysm (dotted line). *Aortic cannula is to the left just proximal to innominate artery, and the heart is to the right.*

In our patient, the contained rupture of the graft took place 12 years postoperatively and resulted in myocardial infarction. We are uncertain as to the cause of rupture. Undetected injury at the time of operation can be ruled out because of the prolonged time frame. The most likely explanation is that intimal fibrosis and hyalinization developed with atherosclerotic changes imposed on the inherent vein wall weakness in valvar areas. At the valves, the usual circular smooth muscle layer of the media gives way to a longitudinal layer of muscle. This is a potential site of weakness [6]. We believe this combination of events led to the formation of an atherosclerotic aneurysm, which spontaneously ruptured.

References

1. Vlodaver Z, Edwards JE. Pathologic changes in aortocoronary arterial saphenous vein grafts. Circulation 1971;44:719–28.
2. Riahi M, Vasu CM, Tomatis LA, Schlosser RJ, Zimmerman G. Aneurysm of saphenous vein bypass graft to coronary artery. J Thorac Cardiovasc Surg 1975;70:358–9.
3. Pintar K, Barboriak JJ, Johnson WD, Co ED. Atherosclerotic aneurysm in aortocoronary vein graft. Arch Pathol Lab Med 1978;102:287–8.
4. Murphy JP, Shabb B, Nishikawa A, Adams PR, Walker WE. Rupture of an aortocoronary saphenous vein graft aneurysm. Am J Cardiol 1986;58:555–7.
5. Shapeero LG, Guthaner DF, Swerdlow CW, Wexler L. Rupture of a coronary bypass graft aneurysm: CT evaluation and coil occlusion therapy. Am J Roentgenol 1983;141:1060–2.
6. Benchimol A, Harris CL, Desser KB, Fleming H. Aneurysms of an aortocoronary artery–saphenous vein bypass graft: a case report. Vasc Surg 1975;9:261–4.

REVIEW OF RECENT BOOKS

Heart and Brain, Brain and Heart
Edited by Prof Dr(Med) Helge Refsum,
Prof Dr(Med) Ilmar A. Sulg, and
Prof Dr(Med) Knut Rasmussen
New York, Springer-Verlag, 1989
470 pp, illustrated, $117.90

Reviewed by Bruce W. Lytle, MD

The cerebral complications of cardiac operations have by necessity been of interest to cardiac surgeons. With today's older and aging cardiac surgical patient population, cerebral complications remain one of the most vexing problems with which cardiac surgeons are faced. *Heart and Brain, Brain and Heart* is a book that is based on a symposium held at the University of Tromso in Norway in June of 1987. The authors state that the purpose of this effort was to integrate basic and clinical aspects of cardiology, neurology, cardiovascular surgery, and neurosurgery, and to a certain extent that has been accomplished. This book is really not likely to be very helpful to practicing cardiac surgeons who are not involved with research.

The chapters that pertain to cerebral function and cardiac surgery constitute less than 20% of the book. There are interesting data presented that relate to cerebral blood flow during nonpulsatile cardiopulmonary bypass, but little clinical correlation. Those chapters that do pertain to clinically related studies involve younger groups of patients, a subset not at particularly high risk for cerebral complications. The chapter by John and colleagues that addresses electroencephalographic monitoring during cardiopulmonary bypass contains pertinent data relating to the monitoring of cerebral function, but again, only anecdotal clinical correlation.

Two important problems cardiac surgeons face today are cerebral complications resulting from atheroembolism and the issues of cerebral protection during deep hypothermia and circulatory arrest. Unfortunately, neither of these subjects is addressed in any detail. I do not think the practicing cardiac surgeon will find this book to be a great deal of help.

Cleveland, Ohio

Squamous Cell Carcinoma Arising in a Sternotomy Scar

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The case of a 73-year-old man in whom squamous cell carcinoma developed in a median sternotomy scar 12 months after coronary artery bypass grafting is presented. A brief review of the literature is included. The etiology of scar carcinoma is discussed and an outline of management given.

(Ann Thorac Surg 1991;51:667–9)

Squamous cell carcinoma frequently occurs in scars, chronic ulcers, and sinuses and as a complication of long-standing granulomas [1, 2]. We report a patient in whom a squamous cell carcinoma arose in median sternotomy scar after coronary artery bypass grafting.

A 73-year-old man had routine coronary artery bypass grafting in June 1986. The skin overlying the sternum was normal. The wound, closed with subcuticular polyglycolic acid sutures, healed without any problem and the patient was discharged after 8 days. One year later he noticed for the first time a small bleeding ulcerated nodule in the wound. Although overlying a sternal wire, the mass was painless and nonpruritic. The lesion was treated as a "sinus" by his family doctor. After 6 months of local treatment the patient referred himself back to our unit.

On examination there was a 2 × 1-cm, hard, ulcerated nodule discharging small amounts of hemoserous fluid. The mass was firmly embedded in the center of the sternotomy scar (Fig 1) and was not adherent to the underlying bone. There were no palpable lymph nodes in the neck or axillae. The patient was admitted for excision biopsy the following day.

At operation the lesion was not adherent to the underlying sternum. There was no sinus or granuloma around any wire. All wires were buried beneath the approximated pectoral muscles. A wide excision was performed and the wound closed primarily after mobilization of the lateral skin margins. The histopathologist reported the lesion as a "keratinizing squamous cell carcinoma. The surgical margins were free of disease" (Fig 2). The wound healed rapidly and the patient remains free from recurrence 12 months later.

Comment

Squamous cell carcinomas are well known to occur in scars, chronic ulcers, sinuses, and granulomas [1, 2]. They are also well known to occur at the site of actinic keratosis on exposed areas [3]. Only a small number arise without exogenous cause [4].

The cause of malignant change in a scar is poorly understood. A depressed immunological state may precede scar carcinoma [5]. The continual repair and regeneration that occurs in marginal epithelium in recurrent ulceration in poorly vascularized scar tissue precedes carcinoma [6]. However even a single injury may produce a scar in which malignancy arises [2]. In such cases previous actinic damage to the skin may have prepared the way for malignant change [1].

Treeves reported "an abnormal relationship between the epithelial and connective tissues in every cicatrix which established a predisposition to cancer formation in those scars which are accompanied by rhagades, ulcers, fistulas and similar chronic lesions" [6]. Persistent pruritis and infection may also predispose to malignant change [6]. Abnormal "metagenic" activity may cause post-burn scars during hyalinization.

The presence of exogenous collagen with fibrinoid change provokes hyperplasia and even invasiveness in the overlying epithelium, which may precede malignant changes [7, 8]. Furthermore, possible stimulation by tissue toxins released by autolysis and heterolysis within scar tissue may be implicated [6].

The carcinoma that occurred in our patient occurred very early in comparison with others in the literature [1, 9–11]. Treeves and Pack [6] have divided scar carcinomas into two groups: acute scar carcinomas, in which the interval between the injury and the cancer was less than 1 year and averaged 0.3 years, and chronic scar carcinomas, in which the interval was 32.5 years.

Acute wound cancers occur more commonly in patients with atrophic or keratotic skin. The ultimate prognosis for acute wound cancers is better than for the chronic carcinomas. Although scar carcinomas occur in younger patients than those carcinomas arising in normal skin, the age of the scar would appear to be more important than the age of the patient [6].

Australia is blessed with a very sunny climate even during the winter. Too many of our population spend many hours exposed to excessive sunlight. As a result we have one of the highest incidences of malignant melanoma in the world. (The incidence of malignant melanoma in Australia varies from state to state.) In New

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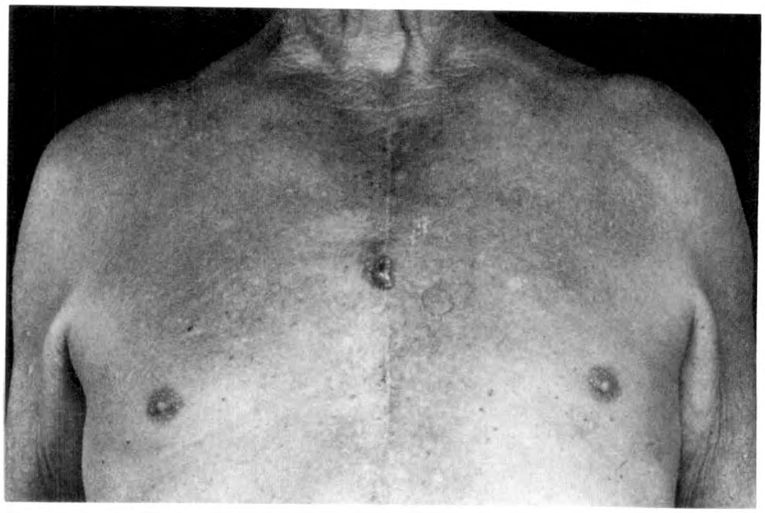

Fig 1. Sternotomy scar at 1 year demonstrating ulcerated nodule in wound.

South Wales the crude incidence per annum is 20 cases per 100,000 male inhabitants and 24.5 per 100,000 women. In Queensland, somewhat closer to the equator, these rates are 26 per 100,000 and 30.1 per 100,000, respectively. By comparison the annual incidence of malignant melanoma in California is 14 per 100,000 men and 11 per 100,000 women [12].

Clearly solar exposure may also be an important causal factor in the development of scar carcinoma in wounds on exposed skin in our environment. However it is less common to see carcinoma (or malignant melanoma) occurring on the chest compared with the face and extremities (ie, exposed areas) even in the caucasian population of Australia. However for many years we have routinely advised our patients not to expose the scar to direct sunlight for at least 12 months.

Conclusions regarding the malignant potential of scar carcinomas are variable and the degree of squamous differentiation does not determine invasiveness [9, 13]. Small superficial epidermoid scar carcinomas of the trunk have a favorable prognosis [1, 14].

Scar carcinomas arising in sun-damaged skin have a low propensity to metastasize [4, 10]. Carcinomas with antecedent lesions are generally less likely to metastasize than those that appear in normal skin [11].

This patient's case is presented to illustrate the potential

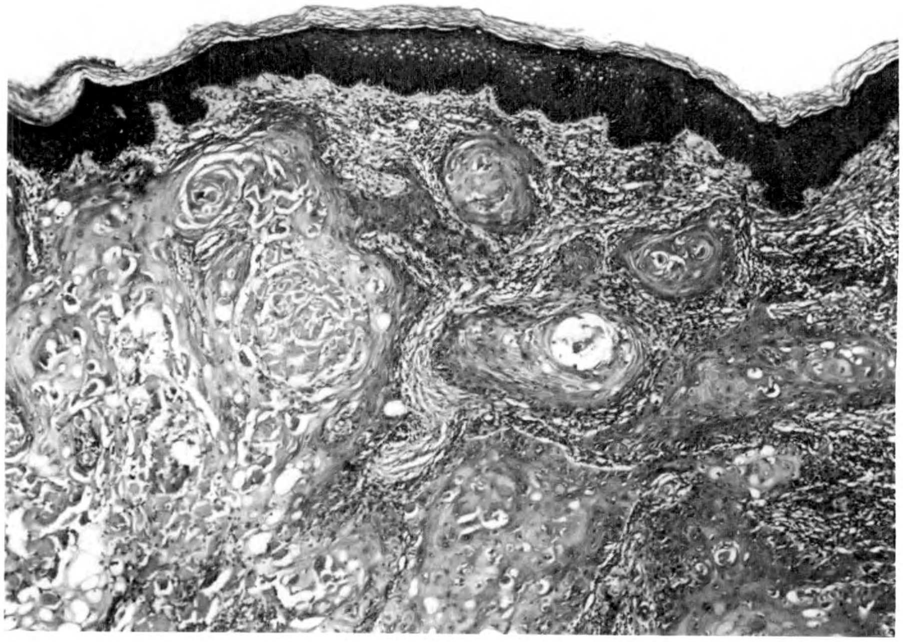

Fig 2. Photomicrograph showing areas of keratinizing squamous cells. (Hematoxylin and eosin, ×4 before 26% reduction.)

for malignant change even in uncomplicated wounds. This potential should be considered in any new lesion occurring after operation.

Early diagnosis (biopsy) and excision offers the best possibility of a cure. Prophylactic dissection of regional lymph nodes is controversial and would only appear justified in those patients with a poorly differentiated lesion that has a predictable route of spread to those nodes being considered for removal [9, 14].

References

1. Cruickshank AH, McConnell ME, Miller DG. Malignancy in scars, chronic ulcers and sinuses. J Clin Pathol 1963;16: 573–80.
2. Mackie RM. Tumours of the skin. In: Rook A, Wilkinson DS, Ebling FJG, Champion RH, Burton JL, eds. Text book of dermatology. 4th ed. Oxford: Blackwell Scientific, 1986: 2431–2.
3. Domonkos AN, Arnold HL, Odom RB. Andrews diseases of the skin. 7th ed. Philadelphia: W.B. Saunders, 1982:825–8.
4. Lever WF, Schaumberg-Lever G. Histopathology of the skin. 7th ed. Philadelphia: J.B. Lippincott, 1975:476.
5. Castillo JL, Goldsmith HS. Burn scar malignancy in a possible depressed immunological setting. Surg Forum 1968;19:511–3.
6. Treeves N, Pack GT. The development of cancer in burn scars—analysis and report of 34 cases. Surg Gynecol Obstet 1930;51:749–82.
7. Gilman T, Bronks D, Penn J, Roux M. Abnormal elastic fibres. Arch Pathol 1955;59:733–49.
8. Sirsat SM, Vandrenalla AM, Khanolkar K. Histochemical and electron microscopy study of epidermal neoplasms. Indian Dermatol Venereol 1963;29:43–7.
9. Stromberg BV, Keiter JE, Wray RC, Weeks MD. Scar carcinoma: prognosis and treatment. South Med J 1977;70:821–2.
10. Graham JH, Bendl BJ, Johnson WC. Solar keratosis with squamous cell carcinoma. A new biological concept. Am J Pathol 1969;55:26A–7A.
11. Glass RL, Spratt JS, Perez-Mesa A. Epidermoid carcinoma of the lower extremity. Arch Surg 1964;89:955–60.
12. Milton GW, Balch CM. Cutaneous melanoma. Clinical management and treatment results worldwide. Philadelphia: J.B. Lippincott, 1985:373, 382, 420.
13. Iregbulem LM. Post burn squamous cell carcinomas in Nigerians. Br J Plast Surg 1987;40:458–93.
14. Shiu MH, Chu F, Fortner JG. The treatment of regionally advanced epidermoid carcinoma of the extremity and trunk. Surg Gynecol Obstet 1980;150:558–62.

Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 16, 1992. The closing date for registration is August 1, 1991.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Excimer Laser Angioplasty During Aortocoronary Bypass Grafting

Carlos Blanche, MD, Jacob Segalowitz, MD, Lawrence S. C. Czer, MD, Scott Wong, MD, and Jack M. Matloff, MD

Division of Thoracic and Cardiovascular Surgery, Department of Surgery, and Division of Cardiology, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California

Laser coronary angioplasty using the 308-nm Excimer laser was successfully performed intraoperatively during coronary artery bypass grafting. It achieved a reduction of the left anterior descending artery stenosis from 99% to 25% as seen on angioscopy, without evidence of vascular perforation or intimal disruption. The Excimer laser offers the opportunity for intraoperative endovascular remodeling and recanalization and has a potential role as an adjunct to existing standard coronary artery bypass grafting protocol.

(Ann Thorac Surg 1991;51:670–2)

Important recent advances involving laser energy and fiberoptic technologies have led us to explore the potential of laser angioplasty to achieve vascular recanalization. The Excimer laser possesses three unique characteristics that may yield a clinical advantage: it ablates by contact without thermal effect [1], it ablates on a pulse-by-pulse basis leaving smooth margins [1, 2], and it is the only laser capable of ablating dense materials such as calcified plaque. Pulsed Excimer laser tissue ablation appears to occur as a discrete event with each pulse, with no visible ejection of material debris. Precision of Excimer laser ablation in vascular tissue is due to several factors: high pulse energy, short pulse duration, limited tissue penetration, and a photochemical decomposition ablative effect [2].

Use of the 308-nm Excimer laser energy through a fiberoptic delivery system became possible and was first applied successfully to revascularize obstructive disease in patients with coronary artery [3, 4] and peripheral vascular disease [5] by a percutaneous approach. This was accomplished after approval for clinical investigation by the Food and Drug Administration and the Cedars-Sinai Human Studies Committee (IRB #610).

The purpose of this report is to describe our initial experience with intraoperative Excimer laser angioplasty during coronary artery bypass grafting.

Case Report

Clinical History

A 61-year-old man was admitted for cardiac catheterization because of recent angina pectoris. This study showed the left main coronary artery had two 30% lesions, and the left anterior descending coronary artery was subtotally occluded proximally (Fig 1). The intermediate circumflex artery had an 80% proximal stenosis, and the obtuse marginal circumflex artery was 40% occluded. The right posterior descending coronary artery had a 90% stenotic lesion at its origin.

On April 11, 1989, the patient underwent intraoperative retrograde Excimer laser angioplasty of the proximal stenotic lesion of the left anterior descending coronary artery during an otherwise routine aortocoronary artery bypass graft operation.

Excimer Laser Angioplasty of the Left Anterior Descending Coronary Artery

A 308-nm xenon-chloride Excimer laser (designed and constructed by the National Aeronautics and Space Administration Jet Propulsion Laboratories and modified for medical applications by Advanced Interventional Systems, Irvine, CA) was used. The laser energy output is up to 250 mJ/pulse with 200 ns pulse duration at a repetition rate of 20 Hz. The designed laser fiberoptic delivery system catheter is 5F in diameter and consists of 12 individual 200-μm pure silica fibers that concentrically surround a lumen designed for passage of a 0.46-mm centered guidewire (Fig 2). The laser is calibrated to emit 308-nm wavelength energy, at 37 mJ/mm^2 per pulse, at a repetition rate of 20 Hz.

Intraoperatively, an arteriotomy was made in the midportion of the left anterior descending coronary artery with the patient on standard cardiopulmonary bypass, and retrograde angioscopy was performed to identify the lesion. Real-time images of the occlusive lesion were videorecorded for documentation. A subtotally occlusive, smooth, nonulcerated atheroma was seen (Fig 3A). The laser catheter loaded with a 0.46-mm guidewire was introduced through the arteriotomy in a retrograde fashion. The guidewire was placed across the stenotic lesion and the laser catheter was advanced over the guidewire and positioned at the most distal end of the lesion. The laser catheter was slowly advanced over the wire across

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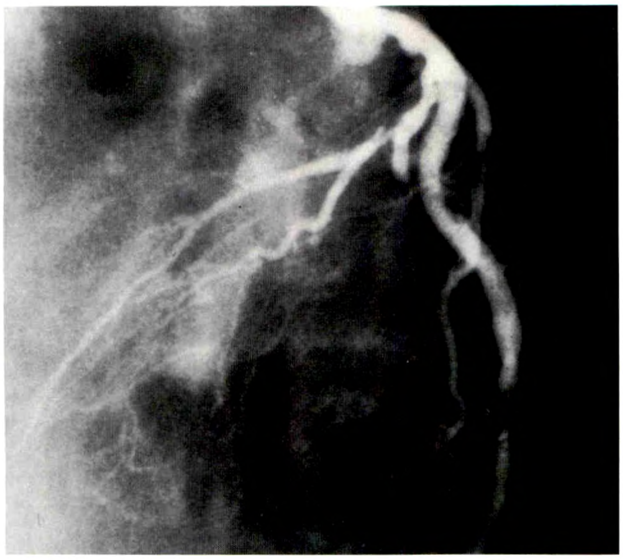
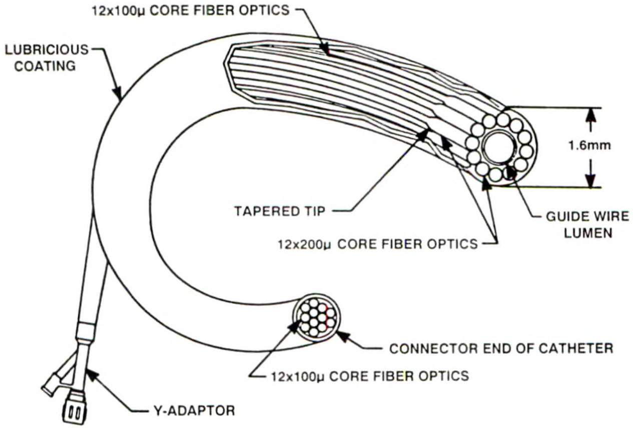


Fig 1. Preoperative angiogram shows the subtotal occlusion of the left anterior descending coronary artery.

the lesion with no resistance; it fired on contact. A total of 1,400 Excimer laser pulses were delivered to the lesion. Repeat intraluminal angioscopy after laser use revealed residual stenosis of 25% with no evidence of disruption of the intima (Fig 3B). This result was also confirmed by videorecorded epicardial coronary echocardiography. The left internal mammary artery was then anastomosed to the left anterior descending coronary artery. The operation was completed in the usual manner with saphenous vein grafts to the right posterior descending, obtuse marginal circumflex, and intermediate circumflex arteries. The patient made an uneventful recovery.

One week after operation, coronary angiography showed the left anterior descending coronary artery open at its laser-treated proximal portion with good filling of its mid and distal portions. Twelve months postoperatively, the patient is asymptomatic.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CONNECTOR END OF CATHETER
12x100μ CORE FIBER OPTICS
Y-ADAPTOR

Fig 2. The laser catheter consists of 12 individual 200-μm pure silica fibers concentrically surrounding a centered lumen for passage of a guidewire.

Comment

The development of laser angioplasty as an efficient adjunct for cardiovascular applications has resulted in increasing scientific interest. Although the use of lasers for recanalization was investigated in the early 1970s, it was only after Gruntzig demonstrated the feasibility of intervention by transluminal balloon angioplasty in the coronary arteries in 1979 that this interest heightened [6].

Laser angioplasty has the potential to help overcome limitations of both balloon angioplasty and bypass grafting. The capability of recanalizing atherosclerotic obstructions may ensure increased long-term patency and reduced restenosis. The intraoperative application of laser angioplasty may permit recanalization in nonbypassable

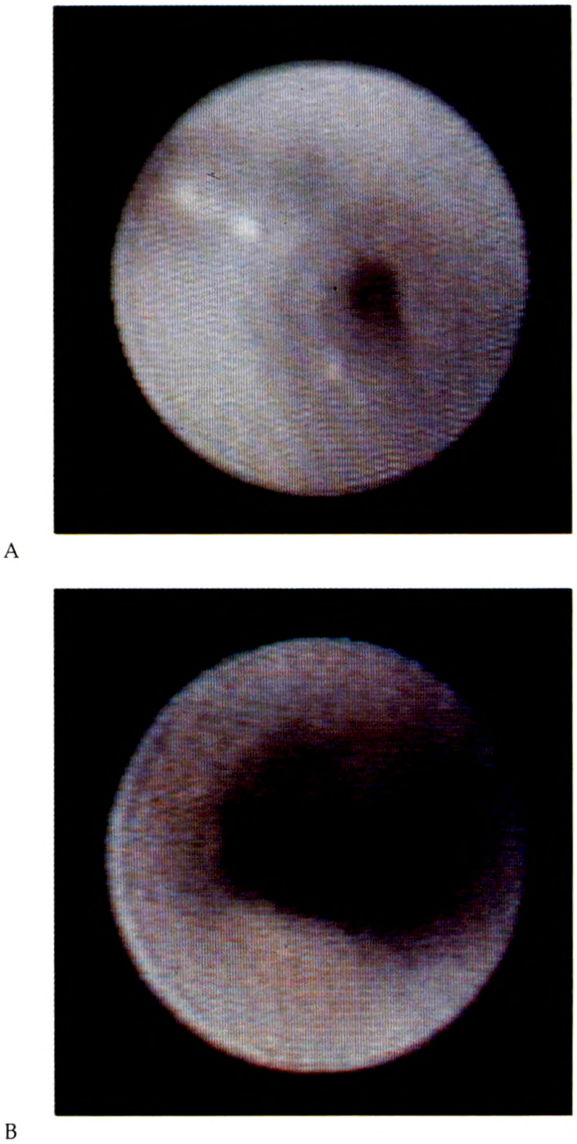

Fig 3. (A) Angioscopic image of left anterior descending coronary artery lesion before laser use. (B) Increased lumen after Excimer laser ablation.

vascular segments of the artery and increase runoff, thus extending and improving the effectiveness of flow in bypassed coronary arteries, achieving a more complete myocardial revascularization. Our first patient treated with intraoperative Excimer laser angioplasty had a reduction of the left anterior descending coronary artery stenosis from 99% to approximately 25%, with satisfactory clinical results.

This case demonstrates the feasibility of 308-nm Excimer laser angioplasty during coronary artery bypass grafting. We believe that this technique will prove to be an effective adjunct to the surgical procedure; however, further experience and long-term follow-up is necessary to define its effectiveness in clinical practice.

We wish to thank Dr Warren Grundfest and Dr Frank Litvack for their technical support, and Kathleen Farrington for her secretarial assistance.

References

1. Segalowitz J, Litvack F, Grundfest W, et al. Direct angioscopic observation of plaque ablation by Excimer laser. Circulation 1989;80:1898.
2. Litvack F, Grundfest W, Goldenberg T, et al. Pulsed laser angioplasty: wavelength power and energy dependencies relevant to clinical application. Lasers Surg Med 1988;8:60–5.
3. Litvack F, Grundfest W, Eigler N, et al. Percutaneous Excimer laser coronary angioplasty. Lancet 1989;2:102–3.
4. Litvack F, Grundfest W, Goldenberg T, Landenslager J, Forrester J. Percutaneous Excimer laser angioplasty of aortocoronary saphenous vein grafts. J Am Coll Cardiol 1989;14:803–8.
5. Litvack F, Grundfest W, Adler L, et al. Percutaneous Excimer-laser and Excimer-laser-assisted angioplasty of the lower extremities: results of initial clinical trial. Radiology 1989;172:331–5.
6. Lee G, Ikeda RM, Kotina J, Mason DT. Laser dissolution of coronary atherosclerotic obstruction. Am Heart J 1981;102:1074–5.

INVITED COMMENTARY

My colleagues and I have performed intraoperative coronary angioplasty with the laser as described by Blanche and associates on two occasions. In both patients the laser catheter was advanced retrograde through a distal arteriotomy and over a guidewire that had been placed through the lesion in the catheterization laboratory before operation. In the first patient, we were able to reduce a subtotal mid-right coronary stenosis to approximately 70% by using a 5F 12-200 catheter. The procedure was uncomplicated and the lesion was easily ablated to achieve a lumen the size of the laser catheter. The second patient had diffuse right coronary disease. In attempting to ablate an 80% stenosis in the mid-portion of the artery we caused a perforation of the vessel. Both patients had routine saphenous vein grafting of the distal artery, and the perforation in the second patient's right coronary artery was easily closed.

From this experience, and from our experimental work with a specially designed intraoperative delivery system, we have concluded that intraoperative coronary laser angioplasty is feasible. Passage of a guidewire before operation is cumbersome and unnecessary. The wire can be passed either antegrade or retrograde through the coronary arteriotomy at the time of operation. Results of laser treatment can be assessed intraoperatively using high-frequency ultrasound or angioscopy.

We agree with Blanche and associates that this exciting new treatment modality may ultimately extend the thoroughness of the revascularization that is achieved with coronary bypass operations. Whether it will improve our patients' long-term outcome can only be answered with large clinical trials.

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Coronary Ostial Reconstruction: Technical Issues

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Coronary ostial reconstruction may be the preferred alternative to reestablish antegrade myocardial revascularization in patients with isolated ostial stenosis. The technical steps of reconstruction are described. The ultrasonic aspirator is a helpful implement in the dissection of the left main and the proximal right coronary arteries. Satisfactory results of coronary ostial reconstruction in the current era seem to fulfill its promise.

(Ann Thorac Surg 1991;51:673–5)

In the early 1980s, Hitchcock and associates [1] revived the procedure of angioplasty of the left main coronary artery (LMCA) for isolated LMCA disease. They introduced the posterior approach in surgical technique. Recently an anterior approach has been reported for LMCA angioplasty [2, 3]. A modified anterior approach was used by my colleagues and me for ostial reconstruction in 3 patients.

Operative Technique

Routine cardiopulmonary bypass with aortic and cavoatrial cannulation, moderate systemic hypothermia (28°C), and hemodilution is employed. Left ventricular venting through the right superior pulmonary vein is extremely important to achieve a bloodless field for final reconstruction. If the patient's condition remains hemodynamically stable it is not necessary to initiate cardiopulmonary bypass after cannulation and one can proceed with dissection.

The ascending aorta is dissected free from the main pulmonary artery (MPA) and the right pulmonary artery. Rubber traction slings are passed around the ascending aorta, MPA, and right pulmonary artery. Two slings around the MPA—one at the level of origin and another at the level of bifurcation—provide better exposure for the dissection of the LMCA. Usually the retraction of MPA and right pulmonary artery and anterior rolling of the aorta provide adequate exposure for the dissection of the LMCA, and partial or total transection of the MPA is not usually needed.

The LMCA is dissected out in its entire length from the aortic origin to its bifurcation, after the epicardial fat over the aortic root is removed and its junction with the ventricular muscle is exposed. For the ease of subsequent plastic reconstruction, it is preferable to extend the dissection to the beginning of both left anterior descending and circumflex arteries. Dissection of the proximal right coronary artery (RCA) is comparatively easier. Proximal 3 cm of RCA is dissected free of fat and neighboring tissues.

Ultrasonic aspirator (Sonoca; Soring, Quickborn, Germany) has facilitated the dissection and exposure of the LMCA and proximal RCA. When used at lower settings of the energy output at the central console, the arteries are delineated precisely without any injury to any structure.

The aorta is cross-clamped and the cardioplegic solution is injected into the aortic root. Usually a single dose of crystalloid hyperkalemic cardioplegic infusion supplemented by topical cooling with iced saline solution is adequate for myocardial protection. However, in the presence of critical stenosis or occlusion of the middle or distal RCA combined with critical stenosis of the left coronary ostium, additional cardioplegic solution will be required to be delivered through a thin, soft catheter introduced after left coronary ostiotomy. Alternatively, retrograde infusion of cardioplegia through the coronary sinus has been used.

The aorta is retracted to the right, the MPA to the left, and the right pulmonary artery is retracted superiorly. If the left coronary ostium is located too far posteriorly, the aorta can be further rolled anteriorly to expose the ostium.

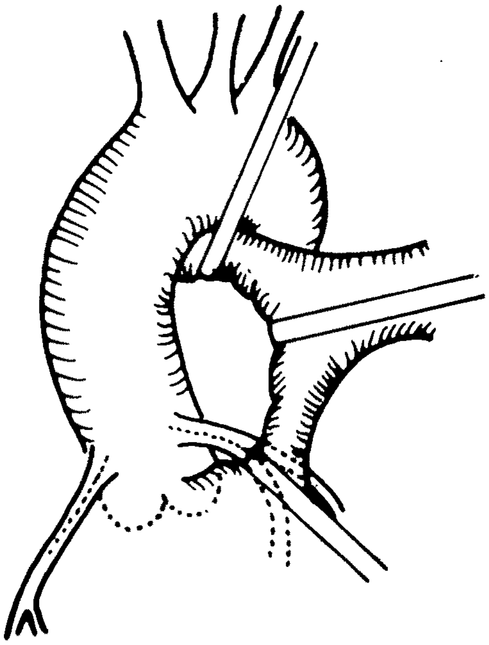

Fig 1. Dotted line *indicates the line of incision of the right coronary artery. The left main coronary artery arteriotomy is extended from the aorta distally.*

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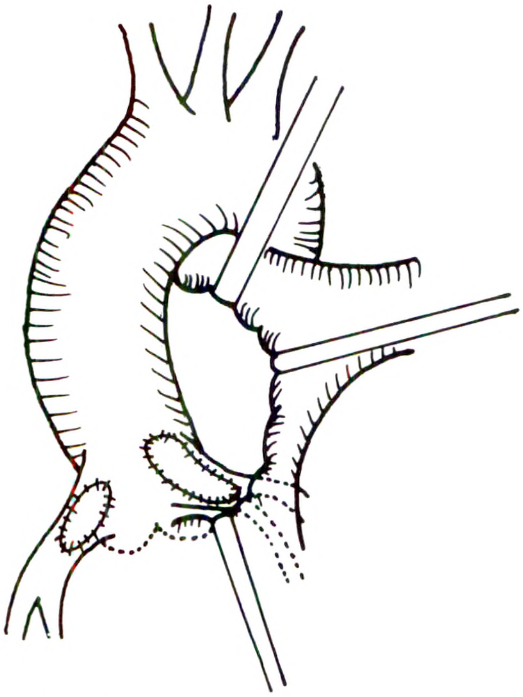


Fig 2. Schematic appearance after bilateral ostioplasty. Note the funnel shape of the reconstructed right ostium.

The aorta is incised longitudinally 1 cm above the ostium. The incision is then extended across the stenosis and along the superior wall of the LMCA up to the bifurcation (Fig 1). Similarly for right coronary ostioplasty, the RCA is incised longitudinally 3 cm below the right ostium, and the incision is continued across the stenosis into the aortic root for 2 cm.

If stenotic irregularity of the posterior wall of the artery is seen after coronary arteriotomy, it can be leveled using the ultrasonic aspirator.

When the left heart is adequately vented, the operative field is usually clear. Low-flow pump run and even transient circulatory arrest have been used for very disturbing coronary backflow [3].

An oblong saphenous venous patch is sewn with a running suture of 7-0 Prolene to the LMCA (or proximal RCA) and with 6-0 Prolene to the aorta. The suture is started from inside out, from the distal end of the arteriotomy incision, and is continued proximally. The enlarged ostium should have a funnel shape. Care must be taken to avoid ballooning or kinking of the onlay patch, especially where the LMCA joins the left posterolateral aortic wall (Fig 2). The cross-clamp is released after dealring.

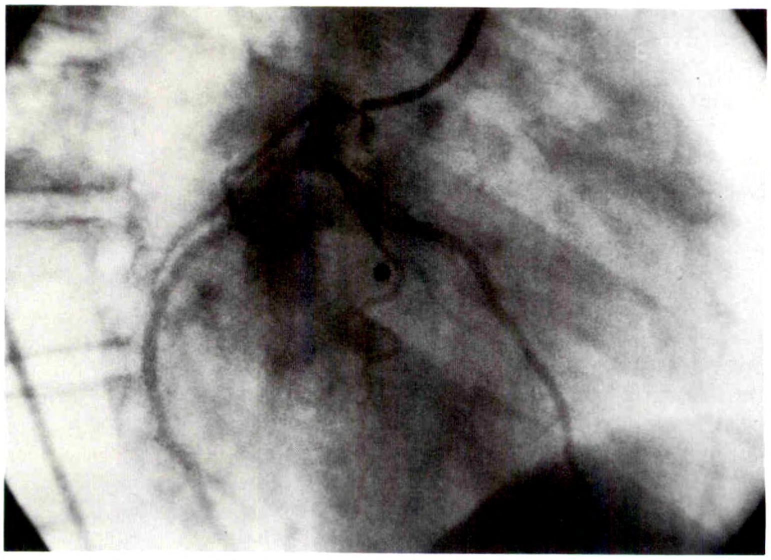
It is important to achieve a water-tight anastomosis and check it while still on cardiopulmonary bypass with near-normal pressure. It is very inconvenient to repair any anastomotic leak after weaning off cardiopulmonary bypass as the reconstructed area mostly disappears out of sight.

Comment

Ostial reconstruction for reestablishing antegrade myocardial revascularization is applicable only in a very small subset of patients with coronary artery disease. Even in this group several contraindications have been recognized [3, 4]. Only about 150 cases of left ostial reconstruction have so far been presented in the world literature. Right coronary artery ostial reconstruction apparently has been attempted in still fewer cases [3, 5].

In our small experience we had very satisfactory results. Both cardiopulmonary bypass time and aortic cross-clamp time were similar to those of conventional coronary artery bypass procedures. Left coronary ostial reconstructions were performed in 2 patients and the right ostial reconstruction in 1. Follow-up angiography (Figs 3, 4) demonstrated a gratifying outcome.

Fig 3. Preoperative angiogram.



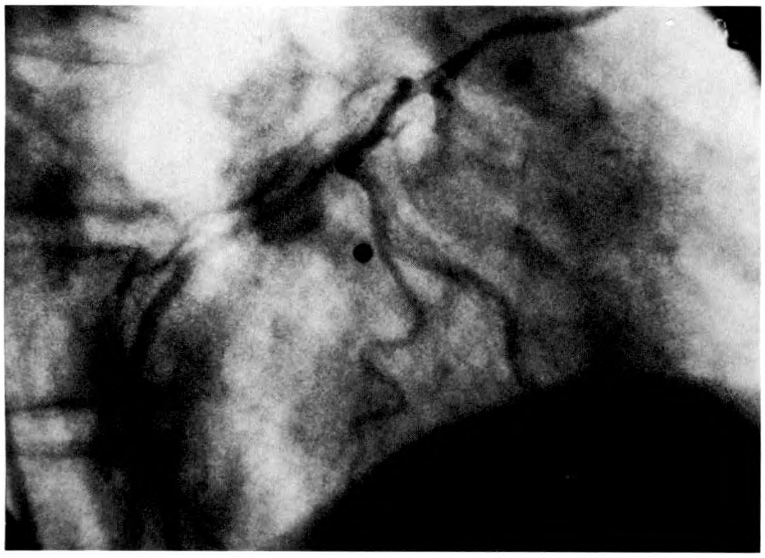


Fig 4. Postoperative angiogram.

Ultrasonic aspirator proved to be a very useful implement both in dissection of LMCA and proximal RCA and in elimination of the stenotic induration of RCA wall. However greater experience is needed to determine its efficacy and its long-term effect as compared with conventional endarterectomy before reconstruction.

Participation of Drs Alber, Isabary, Unger, and others in the clinical management of the patients is acknowledged.

References

1. Hitchcock JF, Robles de Medina EO, Jambroes G. Angioplasty of the left main coronary artery for isolated left main coronary artery disease. J Thorac Cardiovasc Surg 1983;85: 880–4.
2. Sullivan JA, Murphy DA. Surgical repair of stenotic ostial lesions of the left main coronary artery. J Thorac Cardiovasc Surg 1989;98:33–6.
3. Dion R, Verhelst R, Matta A, Rousseau M, Goenen M, Chalant C. Surgical angioplasty of the left main coronary artery. J Thorac Cardiovasc Surg 1990;99:241–50.
4. Ghosh PK, Unger F. Coronary artery reconstructions: why? how? when? In: Ghosh PK, Unger F, eds. Cardiac reconstructions. New York, Berlin, Heidelberg: Springer Verlag 1989: 310–12.
5. Lea JW, Page DL, Hammon JW. Congenital ostial stenosis of the right coronary artery repaired by vein patch angioplasty. J Thorac Cardiovasc Surg 1986;82:796–8.

Patch Aortotomy for Aortic Valve Replacement After Previous Coronary Artery Bypass Grafting

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Exposure for aortic valve operations after previous coronary artery bypass grafting may be technically difficult owing to the presence of patent vein grafts on the proximal aorta. A patch or "island" aortotomy technique that allows excellent exposure of the aortic valve is presented here. In select patients this approach may facilitate cardioplegia administration.

(Ann Thorac Surg 1991;51:676–7)

Exposure for aortic valve replacement or repair after a previous coronary bypass operation may be difficult to achieve with a traditional transverse aortotomy owing to the presence of vein grafts on the proximal aorta. A technique using a patch or "island" of aorta encompassing the proximal vein grafts circumvents this difficulty and in select patients may facilitate cardioplegia administration.

Technique

After institution of cardiopulmonary bypass, the aorta is cross-clamped and cardioplegia administered. Myocardial protection is achieved with antegrade induction and retrograde coronary sinus maintenance. If aortic insufficiency is present, cardioplegia induction is achieved by direct coronary artery cannulation. The left ventricle is vented through the right superior pulmonary vein.

The vein grafts are mobilized off the ascending aorta before application of the cross-clamp. In the presence of bypass grafts to both the right and left coronary systems, a complete patch or "island" of aorta is developed to include all proximal vein graft anastomoses (Fig 1). Further mobilization of the grafts may be necessary to deflect the patch and expose the aortic valve. If grafts to only the left or the right coronary system are present, the patch may be modified. The side of the patch corresponding to the side of the bypass grafts may be left intact. This "flap" of aorta, which includes the proximal vein grafts, may be deflected laterally on the "hinge" of aorta to expose the aortic valve. If the vein grafts are recent and distal coronary embolization of graft debris is not a major concern, cardioplegia may be easily administered by direct vein graft cannulation. Aortic closure is accomplished with patch replacement using a single-layer monofilament suture.

Comment

Aortic valve and coronary artery disease coexist in 20% to 25% of patients [1]. Although routine use of preoperative coronary angiography in patients with aortic valve disease and angina may identify a subset of patients who would benefit from a combined procedure, a small number may require an aortic valve operation after previous coronary artery bypass grafting [2, 3]. Adequate exposure of the aortic valve through a standard transverse "hockey-stick"

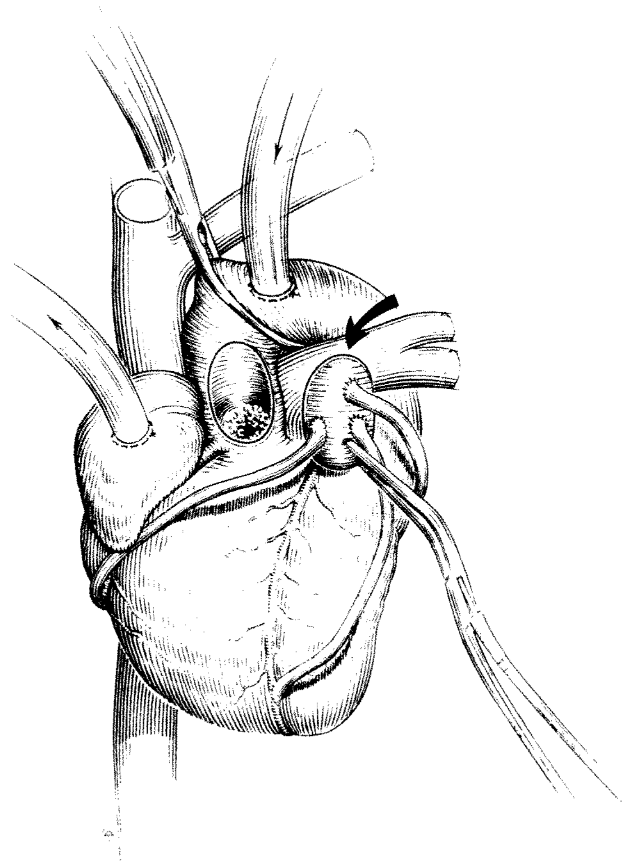

Fig 1. Patch (arrow) *aortotomy for aortic valve operation after previous coronary artery bypass grafting.*

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aortotomy is hindered by extensive scarring and the proximal vein graft anastomoses. A low transverse aortotomy is an alternative approach that may avoid prior vein grafts in select patients. The patch technique described here has been used successfully in 5 patients. It provides excellent exposure to the aortic root while preserving the proximal vein grafts. In select patients this technique may also facilitate administration of cardioplegia.

There are several points that should be emphasized. First, it is our policy to replace vein grafts that are more than 5 years old. However, a small number of patients with aortic valve disease have angiographically "clean" bypass grafts that are less than 5 years old. In our experience, these patients had documented mild to moderate aortic stenosis at the time of coronary bypass not severe enough to require valve replacement. Embolization of cholesterol debris is a concern in any patient undergoing reoperation after coronary bypass grafting. By selecting patients with recently constructed grafts, limiting dissection of the grafts, and using retrograde cardioplegia, the risk of embolization is minimized with this technique. Finally, although the aorta is not normal in patients undergoing reoperation, reimplantation of the patch has been accomplished with a continuous monofilament suture without difficulty.

A new technique for aortic valve exposure in patients with prior coronary bypass grafts is presented. The application of this method to a select group of patients with bypass grafts less than 5 years old is emphasized.

References

1. Basta LL, Raines D, Najjar S, et al. Clinical, hemodynamic, and coronary angiographic correlates of angina pectoris in patients with severe aortic valve disease. Br Heart J 1975;37:150–7.
2. Bonchek LI, Anderson RP, Rosch J. Should coronary arteriography be performed routinely before valve replacement? Am J Cardiol 1973;31:462–6.
3. Lytle BW, Cosgrove DM, Gill CC, et al. Aortic valve replacement combined with myocardial revascularization. J Thorac Cardiovasc Surg 1988;95:402–14.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1993 may begin the recertification process in 1991. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1991. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

The Senning Operation: A New Technique to Prepare the Septal Flap

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We describe a modification of the use of the left atrial appendage for the construction of the new atrial septum in the Senning operation.

(Ann Thorac Surg 1991;51:678–9)

Although the currently preferred treatment for transposition of the great arteries is the arterial switch operation, the Senning operation continues to provide an important alternative in select patients. One of the complications of the Senning operation has been venous pathway obstruction [1, 2], which in part may be due to the use of intracardiac prosthetic material.

After the Rashkind procedure or the Blalock-Hanlon operation, the native atrial septum may be insufficient for use in the Senning reconstruction. Use of the left atrial appendage for the construction of part of the new atrial pathway in the Senning operation has been described [3–5]. We propose a modification of this technique, using the inverted and opened left atrial appendage as an autologous septal flap for the reconstruction of part of the new atrial pathway.

Technique

Cardiopulmonary bypass is carried out as usual for the Senning operation. After aortic cross-clamping and infusion of cardioplegic solution, the right atrium is opened approximately 2 cm anterior and parallel to the interatrial groove toward the crista terminalis superiorly and the eustachian valve inferiorly. Through the opened right atrium, the remnants of the atrial septum are excised completely. The left atrial appendage is then inverted by gentle traction on its apex. Excessive traction may distort the atrioventricular groove, and the subsequent incision may therefore compromise the circumflex coronary artery.

A T-shaped incision is made on the anterior wall of the inverted left atrial appendage (Fig 1). The longitudinal incision is carried from the apex to the base of the appendage and extended transversely, parallel to the appendage-atrial junction. If necessary, some pectinate trabeculae are divided to enlarge the flap. The incision along the base of the left atrial appendage creates an opening that must be closed (Fig 2). The autologous left atrial flap is then sutured along the conventional landmarks to form the floor of the new systemic venous atrium (Fig 3). The remainder of the operation follows the customary routines for the Senning operation.

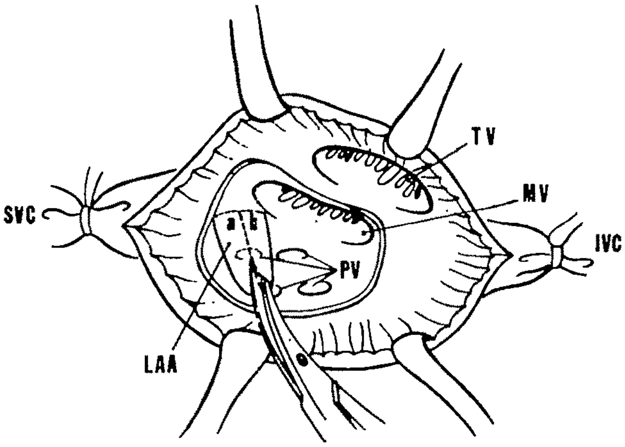

Fig 1. The left atrial appendage (LAA) is inverted and a T-shaped incision is made on the anterior wall. (IVC = inferior vena cava; MV *= mitral valve;* PV *= pulmonary valve;* SVC *= superior vena cava;* TV *= tricuspid valve.)*

Comment

This technique creates a large autologus septal flap, eliminating the use of prosthetic material in the construction

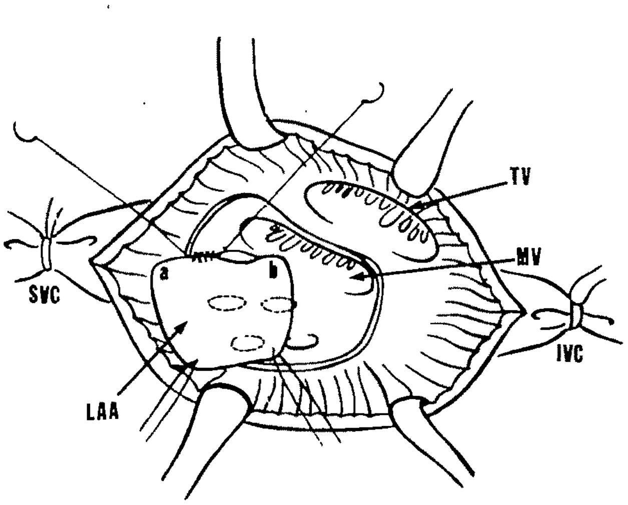

Fig 2. Suture of the opened left atrial appendage (LAA) along the base. (Abbreviations as in Figure 1.)

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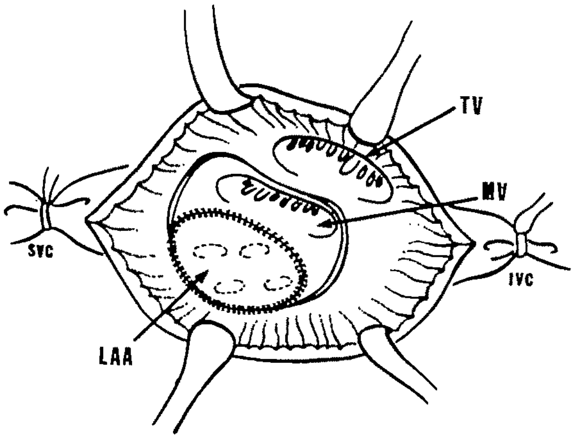

Fig 3. The autologous flap (LAA) is sutured along the conventional landmarks of the atrial septation in the Senning operation. (Abbreviations as in Figure 1.)

of the atrial pathways in the Senning operation. A further advantage is the potential growth of this autologous tissue and perhaps also some contractile capacity of the flap. We have used this technique successfully in a 7-month-old patient with the diagnosis of transposition of the great arteries associated with atrial septal defect. After the operation, two-dimensional echocardiography showed no stenosis of the newly created systemic and pulmonary venous pathways and preserved contractile function of the new atrial septum. The use of this procedure will substantially increase the number of patients who can benefit from the Senning operation without the use of intracardiac prosthetic materials.

We gratefully acknowledge Dr Aldo R. Castaneda and Dr Frank L. Hanley for suggestions during the preparation of the manuscript.

References

1. DeLeon VH, Hougen TJ, Norwood WI, Lang P, Marx GR, Castaneda A. Results of the Senning operation for transposition of great arteries with intact ventricular septum in neonates. Circulation 1984;70(Suppl 1):21–5.
2. Satomi G, Nakamura K, Takao A, Imai Y. Two-dimensional echocardiographic detection of pulmonary venous channel stenosis after Senning's operation. Circulation 1983;68:545–9.
3. Eufrate S, Luisi VS. A further modification of the Senning operation. Thorac Cardiovasc Surg 1981;29:88–90.
4. Hamilton JRL, Wilson N, Dickinson DF, Walker DR. A modification of the Senning procedure for complete transposition. In: Crupi G, Parenzan L, Anderson RH, eds. Perspectives in pediatric cardiology; vol 2. Mt Kisco, NY: Futura, 1989:48–51.
5. Levinsky L, Srinivasan V, Alvarez-Diaz F, Subramanian S. Reconstruction of the new atrial septum in the Senning operation. J Thorac Cardiovasc Surg 1981;81:131–4.

New Operative Method for Distal Aortopulmonary Septal Defect

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A new technique is described for repairing distal aortopulmonary septal defect with aortic origin of the right pulmonary artery in a 26-day-old neonate. To prevent the narrowing of the proximal right pulmonary artery in the distal aortopulmonary septal defect caused by conventional intraluminal prosthetic patch reconstruction, rerouting of the right pulmonary artery using native aortic wall tissue without artificial material was performed. This method seems to be superior to the conventional method, especially during the neonatal period.

(Ann Thorac Surg 1991;51:680–2)

Several surgical approaches have been reported for repair of aortopulmonary septal defect [1–5]. The difficulties of rerouting the right pulmonary artery (RPA) in patients with a distal aortopulmonary septal defect have been considered in the literature [1–5]. Recently, we saw a case of distal aortopulmonary septal defect combined with aortic origin of the RPA and performed a new technique for repairing this anomaly successfully.

Material and Methods

Patient

A 20-day-old neonate was admitted to Tokushima University Hospital with progressive dyspnea. Severe congestive heart failure with increased pulmonary blood flow was present. The chest roentgenogram showed cardiomegaly and pulmonary hypervascularity. The two-dimensional echocardiogram and retrograde aortogram through the left radial artery revealed a large distal aortopulmonary septal defect with aortic origin of the RPA. Neither interruption nor coarctation of the aorta was seen. This patient was operated on on the 26th day after birth.

Surgical Technique

The heart was exposed through a median sternotomy. The RPA arose from the right posterolateral aspect of the ascending aorta (Fig 1A). The right side of the distal part of the main pulmonary artery was connected to the left posterolateral aspect of the ascending aorta at the same height as the RPA. The ascending aorta was slightly tapered from the branching of the RPA.

Cardiopulmonary bypass with the usual aortic and bicaval cannulation was started. The right and left main pulmonary arteries were temporarily snared. During moderate hypothermic bypass, cardioplegic solution was injected into the ascending aorta. A transverse aortotomy was done at the height of the superior ridge of the origin of the RPA (Fig 1B). An ostium in the RPA, 7 mm in diameter, existed at the right posterolateral wall of the ascending aorta, and another ostium, also 7 mm in diameter and communicating to the main pulmonary artery, existed at the same height of the left posterolateral wall of the ascending aorta.

An aortotomy was extended on both sides, bifurcated on the lateral aspect, continued above and below both ostia, and connected to the opposite incisional line on the posterior aspect. Using these procedures, the ascending aorta was transected, and the unroofed RPA was scooped with posterolateral aortic wall tissue to create the anterior roof of the RPA (Fig 1C). The right side of this pulmonary cuff was anastomosed to the left side of the pulmonary cuff with a continuous 6-0 polydioxanone suture without undue tension (Figs 1D, 1E). Finally, the ascending aorta was reconstructed in front of the RPA with another continuous 6-0 polydioxanone suture (Fig 1F). Both great arteries were reconstructed without a prosthesis.

The patient was weaned easily from cardiopulmonary bypass and was extubated on the fourth postoperative day. This patient was discharged on the 38th postoperative day in good condition.

Results

Postoperative cardiac catheterization and pulmonary arteriography were performed in the patient's third month of life. These examinations showed normalization of pulmonary arterial pressure and almost normal formation of the pulmonary tree (Table 1; Fig 2).

Comment

Aortopulmonary septal defect is caused by the faulty embryogenesis of septation of the aortopulmonary trunk. In the type II defect by Richardson's classification, the

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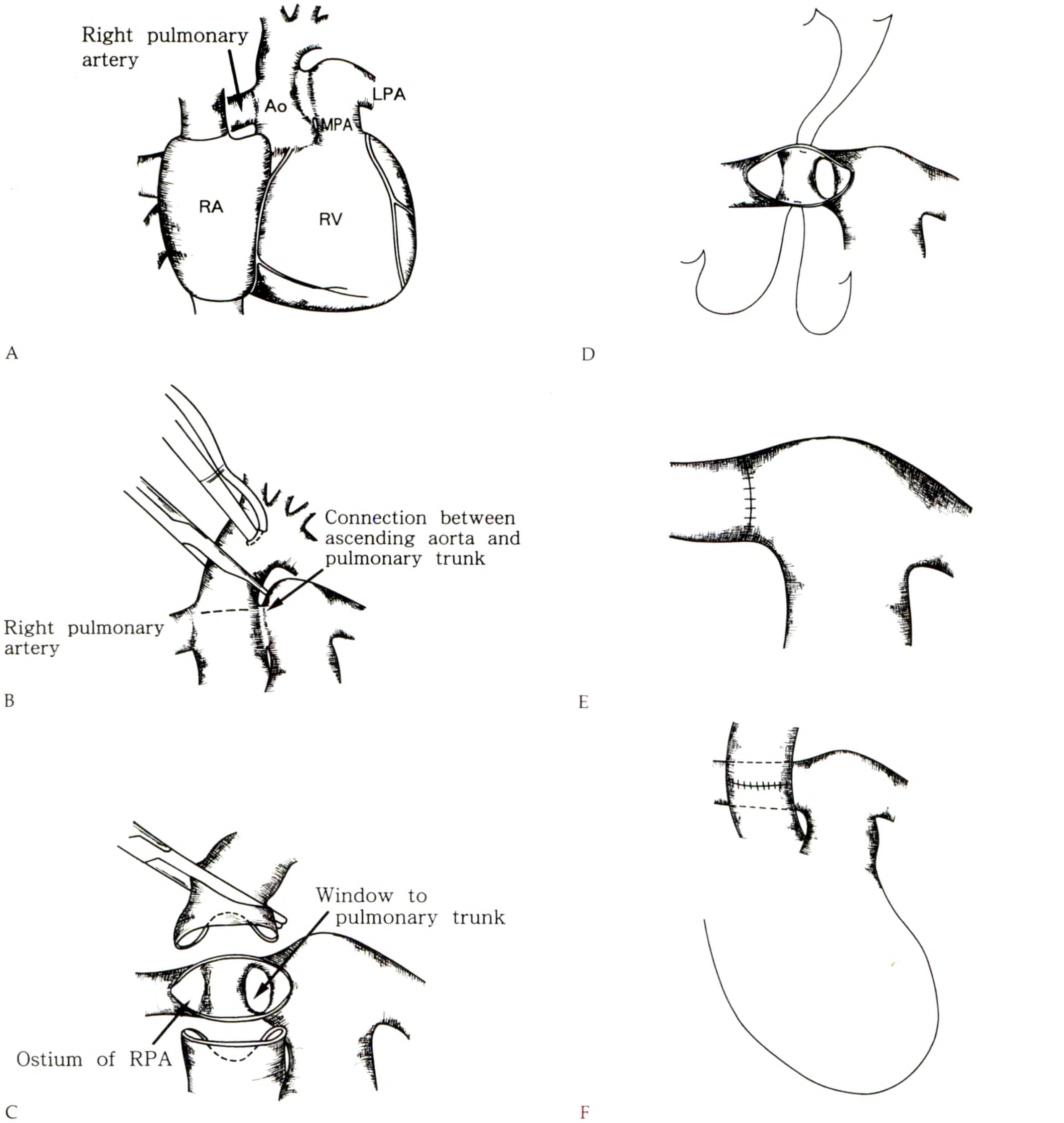
Right pulmonary artery
Ao
LPA
MPA
RA
RV
A
D
Connection between ascending aorta and pulmonary trunk
Right pulmonary artery
B
E
Window to pulmonary trunk
Ostium of RPA
C
F

Fig 1. (A) Right pulmonary artery (RPA) *arising from the right posterolateral aspect of the ascending aorta; left lateral aspect of the ascending aorta communicates with the pulmonary trunk. (B) Usual aortic cannulation.* (Dotted line = *initial incision of the aorta.) (C) Ascending aorta transected; unroofed RPA scooped out of the posterolateral wall of the aorta with aortic wall tissue to create the anterior roof of the RPA: (D) Right side of the pulmonary cuff anastomosed to the left side of the pulmonary cuff. (E) Newly created anterior roof of the RPA. (F) Ascending aorta reconstructed in front of the reconstructed RPA.* (Ao = *aorta;* LPA = *left pulmonary artery;* MPA = *main pulmonary artery;* RA = *right atrium;* RV = *right ventricle.)*

RPA arises from the posterior aspect of the ascending aorta [2]. However, there was a wide distance between the ostium of the RPA and the distal aortopulmonary septal defect in our patient. Therefore, we diagnosed this case as a mixed form of type II and type III defects.

All reports have emphasized the need of early closure of the defect in view of the progression of pulmonary vascular disease [1–5]. Except for special cases, the use of cardiopulmonary bypass and direct visualization of the defect is recommended at the radical operation [1, 3]. The transaortic approach is particularly suitable for all defects [1]. Commonly, it is necessary to reroute the RPA for repairing the type II defect.

In most patients with type II defect, the rerouting of the

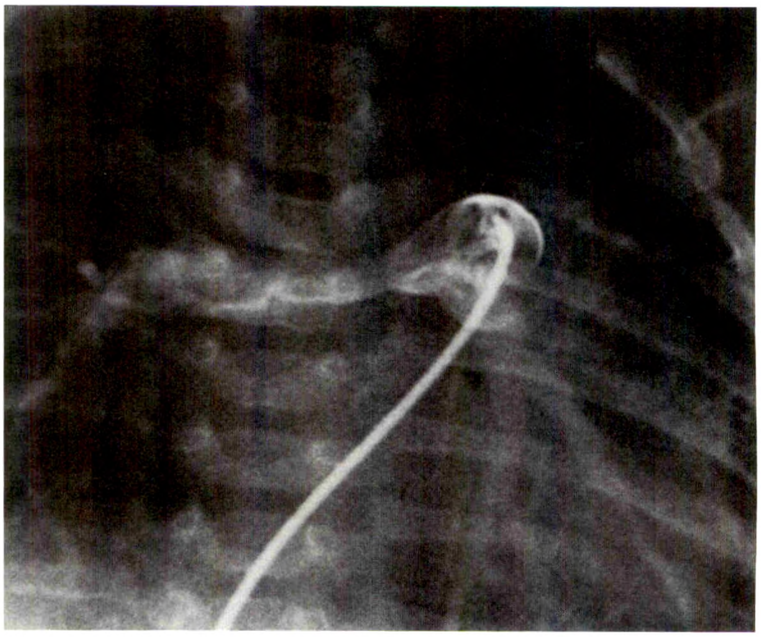

Fig 2. Postoperative pulmonary arteriogram in the patient's third month of life showing almost normal formation of the pulmonary tree.

RPA has been accomplished by intraluminal prosthetic patch reconstruction. Clarke and Richardson [1] used a Dacron patch, shaped like a comma, in a 2-month-old infant. Richardson, Doty, and their co-workers [2, 3] used a contoured Dacron patch in infants. However, this kind of repair for the type II defect, using a prosthetic patch, has not been reported in neonates. The reason is that the prosthetic patch repair in neonates will likely cause narrowing of the proximal RPA in the future. Our new technique with absorbable suture material without a prosthetic patch will allow not only sufficient enlargement but also growth of the reconstructed arteries. For these reasons, we recommend this new procedure for repairing the type II defect, especially in early infancy.

Table 1. Data From Postoperative Cardiac Catheterization in the Patient's Third Month of Life

Site	Oxygen Saturation (%)	Pressure (mm Hg)
SVC	65	(0)[a]
RA	68	(0)
RV	65	34/EDP 5
Main PA	66	34/11 (17)
Left PA	65	33/10 (17)
Right PA	63	14/3 (7)
LV	92	90/EDP 5
Ascending aorta	93	93/50 (60)

[a] Numbers in parentheses are mean pressure.

EDP = end-diastolic pressure; LV = left ventricle; PA = pulmonary artery; RA = right atrium; RV = right ventricle; SVC = superior vena cava.

References

1. Clarke CP, Richardson JP. The management of aortopulmonary window: advantages of transaortic closure with a Dacron patch. J Thorac Cardiovasc Surg 1976;72:48–51.
2. Richardson JV, Doty DB, Rossi NP, Ehrenhaft JL. The spectrum of anomalies of aortopulmonary septation. J Thorac Cardiovasc Surg 1979;78:21–7.
3. Doty DB, Richardson JV, Falkovsky GE, Gordonova MI, Burakovsky VI. Aortopulmonary septal defect: hemodynamics, angiography, and operation. Ann Thorac Surg 1981;32:244–50.
4. Shatapathy P, Rao KM, Krishnan KV. Closure of aortopulmonary septal defect. J Thorac Cardiovasc Surg 1987;93:789–91.
5. Prasad TR, Valiathan MS, Shyamakrishnan KG, Venkitachalam CG. Surgical management of aortopulmonary septal defect. Ann Thorac Surg 1989;47:877–9.

Atrioventricular Valve Replacement With a Hancock Porcine Xenograft

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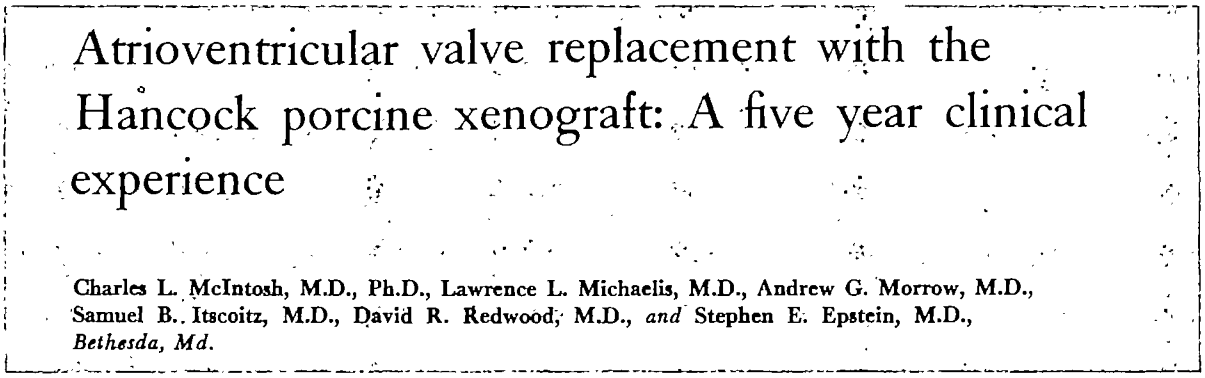
The Hancock porcine xenograft valve was the first commercially prepared, quality-controlled tissue valve. The National Institutes of Health group began implantation of this valve in 1970 and reported on the first 5 years of their results, which was one of the longest follow-ups of that valve at that particular time. Since then there have been a number of centers that have had long-term experience with thousands of these valves. In retrospect, it is now clear that some of the conclusions made by the National Institutes of Health group have not come to pass, such as this valve being the "valve of choice" for all patients. "Valve of choice" is a relative term and may be one valve for one patient and another valve for another patient. This report was important in bringing together some of the first medium-term data and pointing out that, even in this valve, there was some small degree of thromboembolism. The paper also provided a historical look at the methods of data analysis that were in use in the early 1970s compared with those now used in 1991. Actuarial curves were not yet commonly used, nor were percent/patient-year linearized results. Valve types were mixed as well. Hemodynamic data, always a strong point of National Institutes of Health data analysis, were excellent. The use of this valve became a fairly standard device and has been retrospectively analyzed by a number of centers, suggesting that now it is better used in the older patient or in patients who cannot take warfarin sodium. It is a 10- to 15-year valve, less effective in terms of durability in the mitral position than in the aortic. Data still support the original premise that in the patient in sinus rhythm this is an excellent valve replacement device to minimize thromboembolic complications without the benefit of anticoagulation after valve replacement.

(Ann Thorac Surg 1991;51:683–5)



Atrioventricular valve replacement with the Hancock porcine xenograft: A five year clinical experience

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The paper by McIntosh and co-workers [1] from the heart surgery branch of the National Institutes of Health was one of the first medium-term analyses of the porcine bioprosthetic heart valve, and in that regard was a landmark paper establishing for the first time that a commercially prepared biological valve was, in fact, reasonably durable with very low thrombogenicity without anticoagulation. This group was one of six groups (along with Oklahoma City, Stanford, Peter Bent Brigham, Henry Ford Hospital, and University of Padua) that began to use the Hancock porcine bioprosthetic valve in the early 1970s. All have made substantial contributions about bioprosthetic valves over the years, defining the role of the porcine valve in the therapy of valvar heart disease.

The group of 111 patients undergoing mitral or tricuspid valve replacement with this valve reported by McIntosh and co-workers was one of the largest series followed up to that time. The National Institutes of Health had always been known for their very detailed follow-up analysis including postoperative catheterizations of many of the patients undergoing a variety of cardiac operations, and this was no exception. This was also one of the largest series, before or since, of recatheterized patients, 6 months to a year postoperatively, establishing in vivo hemodynamics of this particular valve.

They also documented that long-term durability was clearly better than with any previously commercially

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prepared biological valve, especially formalin-fixed porcine valves. It is interesting to note that at 56 months they had only a single dysfunctional mitral valve and were "unclear" as to why this occurred. As we now know, from several hundred thousand of these valve implants, these valves will calcify but at a much slower rate than previously implanted biological valves such as pericardial or fascia lata valves. As we also now know, from our own work, and from those of many other centers around the world, the porcine valve is a satisfactory valve in the adult patient, particularly the elderly adult, for 10 to 15 years with an increasing dysfunction rate beginning at about 8 years. There are many instances of patients in middle age or older with these valves in place working perfectly well for 12 to 15 years. Unhappily, the valve is a poor choice in the young patient who calcifies these valves in an accelerated fashion. The report by McIntosh and co-workers indicated that durability would be a factor but, in the short term, the valve was seen to be extremely effective. They become enthusiastic, stating in the paper that this valve was "the valve of choice." As we now know, there are many good biological and mechanical valves, and this valve is but one of a number of excellent devices to be used according to the patient's age, medical history, social and economic situation, and anatomical restrictions.

A couple of comments should be made about the data presentation. This group had good follow-up and presented their data in absolute numerical fashion. We note in this paper that there was a lack of actuarial survival curves, hazard functions, and even the outmoded linearized annual incidence of morbidities. It is very refreshing, on the one hand, to read a paper presented in very simplistic, straightforward terms like this, but to get a proper statistical appreciation of any therapy and to put the results of a device or therapy in a proper framework statistically compared with other devices or therapies, we now rely on the more sophisticated techniques such as life-table analysis. It is of interest that the Mayo Clinic and Dr Starr's group in Portland had already been using actuarial curves in their analysis of the Starr-Edwards valve by the late 1960s. The other factor in this analysis that clouded their data somewhat is the fact that they included in their analysis 40 of the 111 patients in whom a prosthetic aortic valve had also been placed. We now know that this is not very good patient strategy, but at the time no one knew the ultimate durability of porcine valves. If a porcine valve becomes dysfunctional in the mitral position, to remove that dysfunctional mitral valve and re-replace it with another valve is a difficult undertaking if an aortic valve is in place, even with the aorta cross-clamped and the heart made flaccid by cardioplegia.

Interestingly, another factor that was mentioned in this article and that has become an important clinical fact is that this group included 2 patients who had documented positive blood cultures and were treated with antibiotics alone and did not require reoperation for endocarditis. This has subsequently been observed many times in patients with porcine valves. With certain bacterial strains (ie, streptococcus), the infected valve leaflets may be sterilized with intense antibiotic therapy rather than reoperation, which is far more common with well-established prosthetic valve endocarditis, which usually involves the annulus.

Another observation that has stood the test of time is their documentation of no hemolysis and no anemia associated with hemolysis that has been seen subclinically, with competent prosthetic valves.

Finally, the changing world of immunology and proper terminology has long since done away with the term "xenograft" in this context. The current term, and one that aptly describes porcine valves, is "bioprosthetic" valve. Xenograft is inappropriate because these porcine valves are not living grafts, but relatively inert collagen shells after treatment with glutaraldehyde. The term "bioprosthetic" was fashioned at the First International Conference on Bioprosthetic Valves, held in Munich in 1979, and has made this an important syntactical clarification ever since.

The porcine valve has been a very useful valve in the therapy of patients with valvar heart disease and has assumed its place relative to other tissue and mechanical valves. It is clearly not the valve of choice in all patients, but I think these investigators at the National Institutes of Health were prophetic in stating that it is a device that would be used for many years, and used very successfully in a large number of patients, especially in the elderly and particularly when anticoagulation is contraindicated.

Reference

1. McIntosh CL, Michaelis LL, Morrow AG, Itscoitz SB, Redwood DR, Epstein SE. Atrioventricular valve replacement with the Hancock porcine xenograft: a five year clinical experience. Surgery 1975;78:768–75.

INVITED COMMENTARY

Dr Cohn makes a number of valid observations concerning the 1975 paper from the National Heart and Lung Institute (NHLI), which reported the medium-term results of the Hancock bioprosthesis used in the atrioventricular positions. There were two follow-up papers from the NHLI tracking the 111 original patients written by Drs Borkon and Foster in 1981 and 1986, respectively, reporting the clinical course, late hemodynamic data, and incidence of valve failure. The reservation expressed in the original paper concerning durability of the bioprosthesis prompted the continued assessment of the valve, and by 1981 our conclusion was that the Hancock bioprosthesis should be used for mitral valve replacement only in patients older than 60 years or in patients with contraindications for anticoagulant therapy. The Foster paper confirmed this philosophy and noted "The high, intrinsic failure rate of the Hancock porcine bioprosthesis after 10 to 12 years has moderated our initial enthusiasm for this valve in the mitral position, and has resulted, in more frequent implantation of mechanical valve substitutes at this institution."

Dr Cohn also noted the methods of data analysis used in the early 1970s did not typically include actuarial curves or percent/patient-year linearized results. Although the original report in 1975, with the mean follow-up of approximately 24 months for the patient population, would not lend itself to meaningful actuarial survival or event-free curves, these methods of analysis were included in the later publications. We strongly endorse the "Guidelines for Reporting Morbidity and Mortality after Cardiac Valvular Operations" prepared by the Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity of The Society of Thoracic Surgeons and the American Association for Thoracic Surgery.

The use of mechanical valves in the aortic position rather than a second bioprosthesis was based on erroneous extrapolation from the experience with the 1000 and 6000 Starr-Edwards ball valves. The incidence of ball variance was many times greater in the aortic position, and we believed that the factors responsible for this would also make the bioprosthesis in this position less durable than in the mitral. Numerous studies have shown that the bioprosthesis is more durable in the aortic position, and we would agree that it is not a good policy to mix mechanical and bioprostheses, except for tricuspid valve replacement, in the same patient. The technical difficulty mentioned by Dr Cohn of doing a redo mitral valve replacement with an aortic prosthesis in place can be less problematic if the mitral valve is approached through either a right anterolateral or left posterolateral thoracotomy rather than a median sternotomy.

The hemodynamic data that accompanied these valve-related papers, as well as all follow-up studies dealing with various acquired and congenital anomalies, were somewhat unique to the Clinic of Surgery, NHLI. Approximately 90% of all patients returned 6 months after operation for evaluation including cardiac catheterization, which added hard data to the longitudinal studies from this unit. Whatever the bond was between patients and the cardiology and cardiac surgical services, they returned religiously, often for serial studies that provided invaluable data in assessing the long-term risk/benefits of an implanted device or specific operation. The NHLI was a repository for these data and the patients who provided it were a "national resource."

Supposed budgetary restraints and redirection of research efforts in what is now the National Heart, Lung, and Blood Institute forced the closing of the surgery branch in July 1990, and with the loss of surgical support, the discontinuation of interventional cardiology. Perhaps noninvasive technology in lieu of catheterization will provide reproducible, hard data that can be used in assessing the immediate and long-term results after an operation or catheter interventional therapy. The explosive development of interventional therapy such as coronary angioplasty, laser, atherectomy, and stent devices will warrant, in the 1990s, well-organized clinical trials similar to those previously conducted by the NHLI. Hopefully extramural funds will be allocated for such studies to provide safety and efficacy data for devices, various forms of interventional therapy, or operations for acquired and congenital anomalies.

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Airway Complications in Relapsing Polychondritis

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To analyze the importance of airway involvement in relapsing polychondritis, an illustrative case report is presented and 62 patients reported in the literature with serious airway complications are reviewed. There were 47 female and 17 male patients, with an average age of 40.3 years (range, 2 to 73 years). Patients were seen with hoarseness, breathlessness, cough, stridor, wheezes, and tenderness over laryngotracheal cartilages. Respiratory tract involvement was confirmed by conventional radiography, tomography, computed tomography, dynamic pulmonary function tests, and bronchoscopy. Corticosteroids and antiinflammatory and immunosuppresive agents were used in these patients. Tracheostomy was performed in 18 patients. Death occurred in 13 patients despite tracheostomy or corticosteroid therapy, or both. A detailed analysis of the clinical, radiological, and pulmonary function studies is presented, with emphasis on upper airway mechanics. The medical and surgical management options are reviewed, including the use of endotracheal prosthesis and extraluminal splinting in dynamic airway collapse.

(Ann Thorac Surg 1991;51:686–92)

Relapsing polychondritis is a multisystemic disorder affecting cartilaginous structures and other connective tissues. Although the term *relapsing polychondritis* was first introduced in 1960 [1], earlier authors described cases of a similar clinical picture. The first reported case has been attributed to Jaksch-Wartenhorst [2], who described a case of polychondropathia in 1923. In 1936, Altherr [3] and von Meyerburg [4] reported cases of chondromalacia involving cartilaginous destruction of the ears, nose, ribs, joints, larynx, and tracheobronchial tree. Although reports have been sporadic, an increasing number of cases have been published since the 1960s. In an extensive review, Hermann [5] collected 452 cases in the world literature reported up to 1986. Since then, a search of the literature revealed a further 113 cases of relapsing polychondritis.

Many excellent reviews of relapsing polychondritis have been published [5–10]. We present an illustrative case report of major airway complications and an in-depth analysis of airway involvement in relapsing polychondritis and its medical and surgical management.

Illustrative Case Report

A 56-year-old man was admitted with increasing dyspnea and productive cough over a 2-month period. Seven years before this he was admitted with intermittent attacks of dyspnea and arthralgia affecting both shoulders, hands, and ankles and the left hip. His pain settled with indomethacin.

On this occasion, examination showed widespread wheezes associated with diffuse crackles. Chest radiography demonstrated perihilar consolidation with hyperinflated lungs. The erythrocyte sedimentation rate was elevated at 95 mm in the first hour but there was no evidence of anemia or serious leukocytosis.

He was given antibiotics and physiotherapy. Over the succeeding few days intermittent attacks of dyspnea associated with cough productive of green sputum developed. A week after admission, the bridge of his nose was noticed to have collapsed. Respiratory function studies, including flow-volume loop (Fig 1), confirmed expiratory airway collapse. Flexible bronchoscopy showed the presence of only three tracheal rings with tracheal collapse on expiration. Immunological investigations confirmed the presence of fetal cartilage antibodies. A diagnosis of relapsing polychondritis was made.

Despite steroids and bronchodilators, his condition continued to deteriorate. Rigid bronchoscopy confirmed tracheal softening and bulging of the posterior membrane of the distal trachea and left main bronchus. A Montgomery T tube with the right limb shortened was inserted. This improved his oxygen saturation considerably. Despite this, he continued to have episodes of severe dyspnea because of his inability to clear secretions through the Montgomery T tube, requiring intensive physiotherapy and suction. He was given cyclosporin A. His condition improved, and he was fit enough to be discharged from the hospital with facility for home suction.

A week later, he was readmitted in severe respiratory distress and septicemia. Chest radiography showed right lower lobar pneumonia. Urgent bronchoscopy confirmed copious secretion with evidence of collapse of the right main bronchus. The Montgomery T tube was removed and a tracheostomy tube inserted. Continuous positive airway pressure ventilation was instituted, resulting in improvement of gas exchange. He was given pulses of methylprednisolone and cyclophosphamide with no response. Because of the lack of success with the Montgomery T tube, posterior membrane fixation of the tracheobronchial tree was considered.

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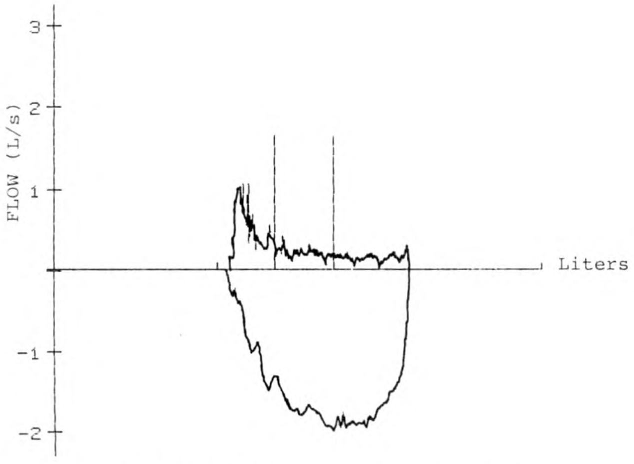

Fig 1. Flow-volume loop showing expiratory airway obstruction.

Through a right thoracotomy, the trachea was mobilized off its mediastinal bed. The trachea, which was small (12 mm in diameter), was grossly inflamed and adherent to the esophagus and the superior vena cava. The posterior membrane of the trachea was found to be folded intraluminally. Careful dissection allowed the mobilization of the trachea and both main bronchi. The left main bronchus, which was the worse affected, was found to be very soft with no residual cartilage, whereas the right was narrowed with some soft cartilage remaining. The posterior membrane of the trachea and both main bronchi was fixed with a Prolene mesh (Ethicon, Edinburgh, UK) covering half the circumference, using Histoacryl tissue adhesive (B. Braun, Germany), thus avoiding sutures to prevent any postoperative air leak. The application of tissue adhesive to the mesh resulted in a rigid sheet on solidification, thus preventing membranous invagination.

Postoperatively his ventilation improved. Repeat bronchoscopy on the third postoperative day showed some inflammation of the mucosa but no collapse of the airway. This was confirmed on dynamic computerized scanning of the trachea (Fig 2), which showed no serious collapse of the distal trachea on expiration. He continued to improve and was weaned off the ventilator on the eighth postoperative day. Over the following 3 weeks he mobilized well and was discharged home on maintenance doses of prednisolone and cyclosporin A.

He remained in reasonable condition for the following 2 weeks but was concerned about his collapsed nose. This was reconstructed with an iliac crest bony implant. Immediately after this procedure, he became dyspneic and went into respiratory arrest. He was therefore reventilated. Bronchoscopy confirmed worsening of the inflammation of tracheobronchial mucosa with copious thick secretions, which were aspirated. His precarious hemodynamic status required the institution of inotropes including dopamine and adrenaline. Over the following month, despite multiple changes of tracheostomy tubes, bronchoscopic clearance, and attempts at internal stenting, his condition deteriorated. Bronchoscopic examinations confirmed progression of inflammation down to lobar and segmental bronchi. He died 3 months after his initial admission. Postmortem examination confirmed extensive destruction of the tracheobronchial tree down to terminal bronchi with gross inflammation.

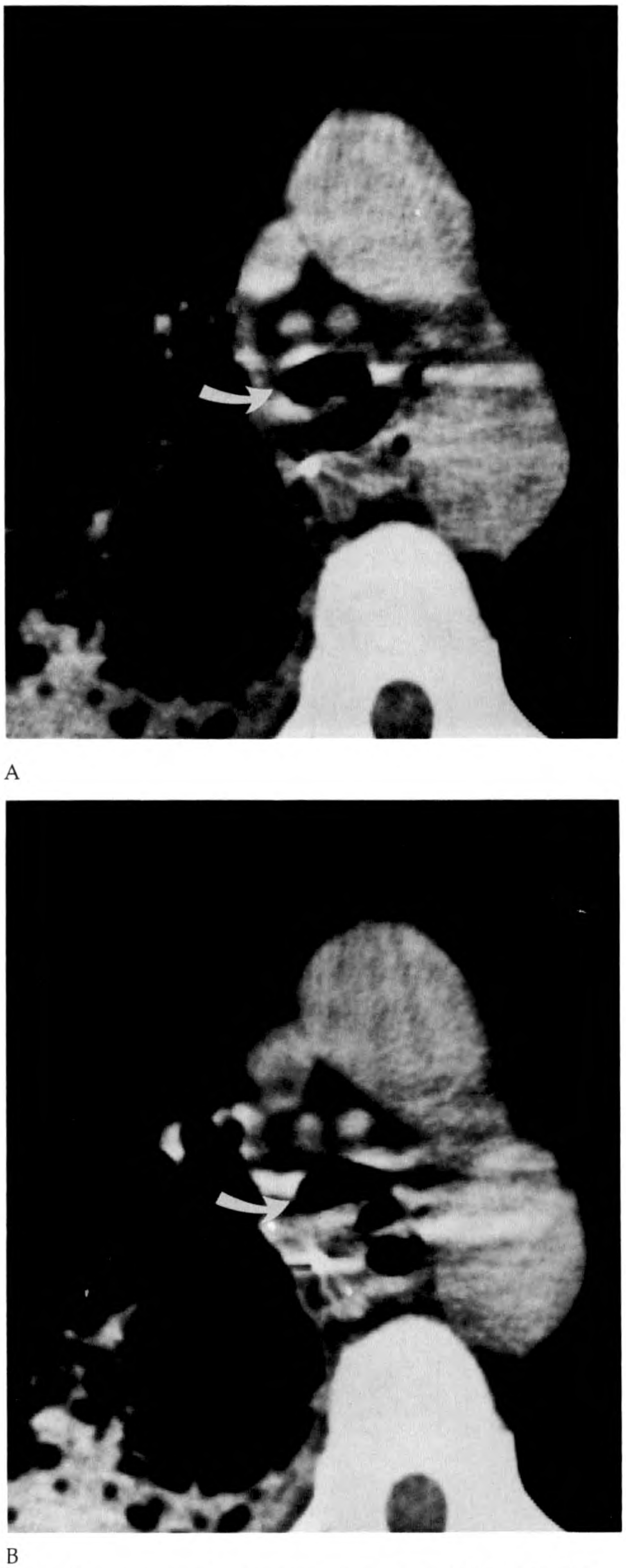

Fig 2. Dynamic computed tomographic scanning of the trachea (arrow) *after posterior membrane fixation (A) on inspiration and (B) on expiration, showing no serious airway collapse.*

Review of the Literature

Clinical Features

Inflammation and destruction of the auricular cartilage, nonerosive arthropathy, and nasal collapse are the most common features of relapsing polychondritis [5–7]. Other structures that may be affected include the eyes [5, 6], cochlear or vestibular structures [6], cardiac valves [11], large vessels [12], and the kidneys [13]. Involvement of the respiratory tract, although relatively unusual when the patient is first seen [6], becomes more frequent as the disease progresses. Respiratory involvement as an initial symptom has been reported in 13% [9] to 26% [8], whereas eventual involvement occurs in up to 50% of patients [6]. Respiratory tract complications account for significant increases in clinical morbidity and mortality [6, 10].

Of the 62 cases reported in the literature with serious airway involvement and sufficient details for analysis [1, 6, 7, 10, 14–28], there was a preponderance of female patients (F:M = 45:17) with an average age of 40.3 years (range, 2 to 73 years). The sex ratio is at variance with that reported in all cases with or without respiratory involvement, which have an equal sex prevalence [5]. As in other cases, patients with respiratory involvement may be at each extreme of ages.

Airway involvement in relapsing polychondritis may be diffuse or localized [6] and may involve the upper extrathoracic airway, intrathoracic trachea, or even bronchi. In this series of 62 patients, however, laryngeal and upper tracheal involvement was more common, being present in 42 cases, with 18 cases involving the whole trachea and 4 involving the left main bronchi only. This may be a reflection of incomplete assessment, however, because detailed airway investigation including the use of computed tomography has revealed more extensive involvement of the lower airway even in patients not suspected of having such involvement [23].

When first seen most patients have breathlessness (n = 31), with hoarseness (n = 20), cough (n = 20), stridor (n = 13), tenderness over laryngotracheal cartilages (n = 9), and wheezes (n = 5) the other features suggesting airway involvement. Although all cases of subglottic strictures [29] and tracheal stenosis [10] are symptomatic, lower airway disease may be asymptomatic and is found only on tomography and pulmonary function testing [29].

Pathophysiology of Airway Involvement in Relapsing Polychondritis

Respiratory disturbances in relapsing polychondritis may be the result of major airway collapse secondary to a destruction of the cartilaginous rings or narrowing secondary to inflammatory edema and cicatricial fibrosis [23]. This has been confirmed by pulmonary function studies to be predominantly due to airway abnormalities and not to the loss of elastic recoil forces of the lungs [5]. Pulmonary infections ensue from impaired clearance of airway secretion as a result of disruption of the mucociliary escalator at the site of inflammation or scarring and diminished effectiveness of cough in clearing secretions from the lower respiratory tract as a result of dynamic upper airway collapse [22]. Tracheal collapse may occur suddenly, causing rapid death [10]. It may also be induced by bronchoscopy or intubation [6] or by tracheostomy [14].

Radiological Investigations

Conventional radiography and tomography have been the methods of radiological investigations for airway involvement in relapsing polychondritis. These may reveal narrowing of the trachea and the complications of airway obstruction and collapse. In recent years, the use of computed tomography has allowed better demonstration of laryngotracheal involvement [23, 28]. The use of thin-section computed tomography has shown that even lobar and segmental bronchi may be involved in the disease process [28]. However, even though cartilage may be present in airways down to 1 mm in diameter, it is of less importance for bronchial stability in these smaller pulmonary airways, which are supported by the surrounding lung, and its loss should produce little effect on pulmonary functions [18]. Cinebronchographic studies may define collapse of airway more effectively [5, 30]. In patients with stridor resulting from marked narrowing of the airway, the instillation of contrast material into the larynx and trachea may further compromise the caliber of the narrowed lumen [19]. This may result in acute dyspnea at the time of the examination. The avoidance of contrast instillation in dynamic computed tomographic scanning of the upper airway is particularly useful in such cases.

Airway Mechanics

The functional effects of respiratory tract involvement depend not only on the location of the obstruction but also on whether the lesion is fixed or dynamic. The location is most important in dynamic obstruction because intrathoracic lesions behave differently from extrathoracic ones [31]. During inspiration, the intraluminal pressure in the extrathoracic airway is subatmospheric while extraluminal pressure is approximately atmospheric. This favors narrowing of the extrathoracic airway, and thus a dynamic lesion in the extrathoracic airway will cause maximal derangement on inspiration [31]. Further narrowing may occur as a result of airflow turbulence and the acceleration of the air by the Bernoulli effect [32]. On expiration, however, the intraluminal pressure is positive relative to extraluminal pressure in the extrathoracic airway, which tends to dilate the airway and obscures the presence of the lesion. Thus a variable extrathoracic lesion will cause a predominant decrease in maximal inspiratory flow.

On the other hand, when the dynamic obstruction is in the intrathoracic airway, the maximal effect occurs during expiration because during expiration the extraluminal pressure is positive relative to intraluminal pressure in the intrathoracic airway, tending to collapse such an airway [31]. This effect is exaggerated during coughing because a greater pressure gradient is generated after opening of the glottis [30].

The nature of the airway obstruction can be assessed by pulmonary function studies. Conventional spirometric tests have not been very helpful in distinguishing the different types of airway obstruction. The use of flow-volume curves has been helpful in many instances [33, 34]. Fixed obstruction causes a significant reduction of both inspiratory and expiratory airflow [22]. A dynamic obstruction in the extrathoracic airway tends to have maximal effect on inspiration whereas a dynamic lesion in the intrathoracic airway, on expiration. This may be quantified by the ratio of the maximal expiratory to maximal inspiratory flow at mid-vital capacities [22, 34]. An analysis of the flow-volume loops helps in defining the nature of the obstruction, whether fixed or dynamic, and the location, whether intrathoracic or extrathoracic. It is invaluable not only in planning management of the patients but also in monitoring progress of the disease [34].

Further assessment of the severity of airway involvement in relapsing polychondritis may be made by direct measurement of airway resistance by body plethysmography [18, 22].

Bronchoscopy

Bronchoscopy is useful in elucidating the nature and severity of airway involvement in relapsing polychondritis. It does carry a serious risk, however. Deaths have occurred during the procedure [16]. The margin of safety that exists in a patient with chronic asphyxia is very narrow indeed [14]. Bronchoscopy may reveal severe inflammation of the trachobronchial tree [25] or collapse of the major airways, which open easily on passage of the bronchoscope but collapse on withdrawal [17].

Diagnosis, Pathology, and Etiology of Airway Involvement in Relapsing Polychondritis

There are no laboratory tests specific for relapsing polychondritis. Diagnosis therefore depends on the clinical features, which have been well described [5, 6], including its association with the involvement of the ears, nose, joints, skin, and special organs including the major vessels, eyes, heart valves, kidneys, and the brain. McAdam and associates [6] established the diagnostic criteria for relapsing polychondritis. There is increasing evidence of the immunological nature of this disease with demonstration of antibodies to type II collagen [35] and cell-mediated immunity [36]. The observation of a placental transfer of relapsing polychondritis with an affected child and subsequent recovery of the offspring suggests an important role of the antibody in this condition [37]. A case of hydralazine-induced relapsing polychondritis has been reported [21]. Experimental animals demonstrated collapse of cartilage after intravenous injection of papain [38] and sensitization to type II collagen [39].

Biopsy of cartilaginous lesions in relapsing polychondritis reveals loss of basophilic staining of matrix, associated with infiltration of polymorphonuclear leucocytes, lymphocytes, monocytes, and plasma cells [5, 6]. On electron microscopy, the chondrocytes contain large quantities of lysosomes, lipid, and glycogen. Such cells and adjacent collagen may be destroyed and replaced by small electron-dense granules and vesicles that vary in size, shape, and density [5]. Tracheal mucosa frequently appears edematous. Its cartilaginous rings show changes ranging from mild inflammation to total resorption by granulation tissue [5].

Further laboratory investigations may reveal an elevated erythrocyte sedimentation rate, moderate leukocytosis, thrombocytosis, eosinophilia, and normocytic and normochromic anemia [5]. An elevated erythrocyte sedimentation rate is a direct index of the activity of the disease and is a guide in controlling dosage of drugs [20]. The erythrocyte sedimentation rate may be normal, however, in patients with relapsing polychondritis [6]. Urinary analysis may reveal an elevated level of acid glycosaminoglycans [40].

Differential Diagnosis of Airway Involvement in Relapsing Polychondritis

In addition to relapsing polychondritis, tracheal stenosis may result from trauma associated with endotracheal intubation, infections and noninfectious granulomatous reactions in the mediastinum, neoplastic disease, the use of β-blockers, the saber-sheath trachea associated with chronic obstructive pulmonary disease, and tracheobronchopathia osteochondroplastica differentiated by calcified mucosal nodules projecting into the lumen of the trachea or main bronchi [5]. Airway collapse may result from idiopathic tracheomalacia, compression of trachea by goiter, emphysema, or congenital chondromalacia of the trachea. The association of airway involvement with the other features of relapsing polychondritis suggests its diagnosis on clinical grounds [6].

Medical Management

Most cases of relapsing polychondritis can be managed medically, even in patients with airway involvement. The mainstay of treatment remains corticosteroids. Most patients first receive moderate doses and may require large doses during periods of intense disease activity [6]. In the respiratory tract, corticosteroids have been noted to help the acute laryngeal inflammation that may occur early in the disease but do not help in the later-developing loss of cartilaginous support [5, 6]. Corticosteroids were used in all the patients analyzed in this series of 62 patients. Milder disease may be managed with the use of dapsone, aspirin, and other nonsteroidal antiinflammatory agents [5].

Success has also been reported with the use of immunosuppressive agents including azathioprine [6, 22, 27], cyclophosphamide [5], 6-mercaptopurine [6], penicillamine [27], and cyclosporin A [6, 41]. Cyclosporin A has been shown to be effective in reversing airway narrowing when steroids and cyclophosphamide are ineffective [41]. Because antibodies seem to be important in the pathogenesis of the disease, plasmapheresis may have a role in the management of these patients [24].

Surgical Management

Tracheal cartilage may suddenly collapse, causing rapid death [10]. Early tracheostomy has been recommended in patients with airway obstruction from relapsing polychondritis, but this is likely to benefit only patients with localized subglottic involvement [18]. It has been found, however, that endoscopy and intubation are fraught with hazard, may precipitate a sudden marked increase in dyspnea, and have led to death on occasion. Early tracheostomy should therefore be performed if indicated rather than procrastination with bronchoscopy or intubation [6]. Tracheostomy itself may carry a serious risk by inducing fatal airway obstruction [14]. The small glottis resulting from cartilaginous destruction may make intubation difficult during anesthesia. A small endotracheal tube may have to be used. Once this has been achieved, adequate ventilation may be maintained even in patients with complete reversible airway collapse by the use of positive-pressure ventilation. This then allows careful assessment of the airway and planning of further medical and surgical management.

Although major advances have been made in the surgical management of tracheal tumors and strictures by resection and reconstruction [42], the results of surgical excision of inflammatory lesions are not good [43]. Surgical resection of subglottic strictures has been attempted in 2 cases [15, 26] and appeared to produce good results. Both patients still required intensive medical therapy, however, and 1 required the insertion of a Montgomery T tube.

Use of Endotracheal Prosthesis

The use of the Montgomery T tube [44] and its modifications [45] has allowed greater flexibility and success in the management of neoplastic, postintubation stricture, and anastomotic complications. Its use in patients with airway collapse and narrowing secondary to relapsing polychondritis is still relatively rare. For patients requiring prolonged tracheostomy, however, the insertion of an endotracheal stent allowed the retention of voice. Its use up to 4 years has been satisfactory. Unfortunately, progression of disease, as in the case of tracheomalacia, resulted in four deaths out of 5 patients with an intraluminal stent for airway collapse [45]. The possible displacement of the stent may lead to asphyxial crisis. Its erosion through the tracheal wall into the innominate artery has caused death from massive hemorrhage [44]. Irritation of the mucosa causing ulceration and granulation tissue formation and aspiration pneumonia when the upper limb projects through the vocal cords are other known complications [46]. Inability to cough effectively due to length of the tube leads to retained secretion and infection. Septicemia may result, as in our patient.

Airway Splinting

Dynamic obstruction from central airway collapse in relapsing polychondritis may be amenable to airway splinting [18]. Bronchoscopic assessment of such patients may reveal the prolapse of the posterior membraneous wall [24]. External splinting by suspension to vascular adventitia and percutaneous sutures has been successfully used in airway collapse from tracheomalacia after thyroidectomy [47]. Success in circumferential and posterior membrane stabilization has been described for airway collapse from tracheomalacia [47] and emphysema [48]. The extent of stabilization required, either posterior membrane or total stabilization, may be determined by the extent of the disease [48]. In many cases, support of the posterior membrane suffices [49]. There is a danger in converting the trachea into a stiff, rigid tube, which may be catastrophic in terms of airway clearance [49]. Support of the cartilaginous tracheal rings without the posterior membrane has also been used in tracheal collapse in emphysema [50].

The materials used in splinting include pericardium, dura mater, and skin grafts [51]. Gore-Tex mesh has been found particularly useful [51, 52]. To avoid the use of sutures on the posterior membrane, which may lead to air leak, tissue adhesive has been applied successfully [52]. The use of tissue adhesive by itself has been found not to be sufficient [53].

In the presence of extensive tracheobronchial involvement in relapsing polychondritis, external airway splinting is the treatment of choice. This can be achieved through a right thoracotomy, which allows access to the trachea and both bronchi. Posterior membrane fixation using tissue adhesive [54] can be effectively achieved.

Prognosis of Patients With Airway Involvement in Relapsing Polychondritis

In most patients with relapsing polychondritis, it is probably reasonable to evaluate the upper airway with a combination of techniques including computed tomography, bronchoscopy, and flow-volume loops [55]. Although most patients with relapsing polychondritis have features of multisystemic, multiorgan involvement, airway involvement in relapsing polychondritis can occur without apparent clinical involvement of the ear or nasal cartilage [55]. Airway involvement has been the main cause of death in most series reviewed [1, 6, 9, 10], being involved in up to 50% of patients. However, some authors reported death from respiratory tract involvement in only 10% of their patients [8]. In general, it can be accepted that the high frequency of respiratory involvement, in up to 50% of patients [6], accounts for substantial morbidity and mortality in patients with relapsing polychondritis. Survival rates of 74% at 5 years and 55% at 10 years have been reported [8]. Young patients with laryngotracheal involvement when first seen have a worse prognosis than those in whom respiratory signs developed later in the course of the disease as they do not respond as well to steroids [27].

In this review of 62 patients with respiratory tract involvement, death occurred in 13 (20%), 6 of whom died at or after tracheostomy and 4 despite prolonged steroid therapy, confirming that disease progression may occur even with steroid treatment.

Summary

Relapsing polychondritis is a disease manifested by recurring episodes of inflammation in cartilaginous tissues throughout the body. The coexistence of various rheumatic and autoimmune disorders in 30% of patients has led to the suggestion that an immunological dysfunction may be involved in the pathogenesis of relapsing polychondritis. These disorders include systemic vasculitis, rheumatoid arthritis, Sjogren syndrome, systemic lupus erythematosis, Behçet's disease, ankylosing spondylitis, and Reiter's disease [5].

The disease is characterized by episodic painful inflammation of the cartilage, most commonly in the outer and inner ear, nose, costochondral junction, and a variety of joints, and in some cases it involves the cartilage of the respiratory tract [56]. In about a third of cases, the disease begins with the involvement of the pinna, which is eventually affected in 86% of the patients [56]. Cauliflowerlike ears result from recurrent inflammation, scarring, and retraction. The nasal cartilage is involved in about three quarters of the cases, typically resulting in a saddle nose deformity. The diagnosis of relapsing polychondritis can be made on clinical grounds when three or more of the following features are present [6]: (1) bilateral auricular chondritis, (2) nonerosive, seronegative inflammatory polyarthritis, (3) nasal chondritis, (4) ocular inflammation, (5) respiratory tract chondritis, and (6) audiovestibular damage.

Although the disease is thought to be rare, more than 600 cases of relapsing polychondritis have been reported in the world literature. It has been reported predominantly in white patients but has been described in all races. There is an equal sex prevalence with the majority of cases appearing in patients between the ages of 40 and 60 years [5]. In this analysis of patients with serious respiratory tract involvement, there is a female preponderance, although the ages of the patients correspond to those reported generally.

Respiratory tract involvement from airway narrowing or collapse occurs in up to 50% of patients with relapsing polychondritis [6], although when first seen they may not have symptoms referable to the upper airway. The presence of hoarseness, cough, breathlessness, stridor, wheezes, and tenderness over the laryngotracheal cartilages suggests the possibility of airway involvement. Adequate assessment using conventional radiography, tomography, computed tomography, dynamic pulmonary function studies (especially flow-volume curves), and bronchoscopy is necessary before a rational therapeutic option is arrived at. Most patients with airway involvement respond to medical therapy with corticosteroids and antiinflammatory and immunosuppressive agents. Localized strictures are treated by dilation and stenting or resection and anastomosis. Reversible airway collapse can be managed, in carefully selected patients, by the use of extraluminal splints, particularly posterior membrane stabilization performed through a right thoracotomy. The use of tissue adhesive in such a procedure not only obviates the use of sutures, which can lead to air leak, but also allows a firmer posterior membrane fixation on solidification.

In conclusion, in select patients with airway collapse caused by extensive tracheobronchial involvement in relapsing polychondritis, posterior membrane fixation in addition to immunosuppressive therapy should be the treatment of choice. Tracheostomy alone without continuous positive airway pressure has no role in such cases. The problems with intraluminal stents mean that these have a very limited role in the long-term management of such patients. Exacerbation of immune response may follow operation on cartilaginous structures including the nose and, hence, this is best avoided.

References

1. Pearson CM, Kline HM, Newcomer VD. Relapsing polychondritis. N Engl J Med 1960;263:50–8.
2. Jaksch-Wartenhorst R. Polychondropathia. Wien Arch Intern Med 1923;6:93–100.
3. Altherr F. Uber einen Fall von systematisierter Chondromalacie. Virchows Arch Pathol Anat 1936;297:445–79.
4. Von Meyerburg R. Ueber Chondromalacie. Schweiz Med Wochenschr 1936;17:1239.
5. Hermann JH. Polychondritis. In: Kelley WN, Harris ED, Ruddy S, Sledge CB, eds. Textbook of rheumatology. 3rd ed. Philadelphia: W.B. Saunders, 1989:1513–22.
6. McAdam LP, O'Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. Medicine 1976;55:193–215.
7. Kaye RL, Sones DA. Relapsing polychondritis. Clinical and pathological features in fourteen cases. Ann Intern Med 1964;60:653–64.
8. Michet CJ, McKenna CH, Luthra HS, O'Fallon WM. Relapsing polychondritis. Survival and predictive role of early disease manifestations. Ann Intern Med 1986;104:74–8.
9. Hughes RAC, Berry CL, Seifert M, Lessof MH. Relapsing polychondritis. Three cases with a clinico-pathological study and literature review. Q J Med 1972;61:363–80.
10. Dolan DL, Lemmon GB, Teitelbaum SL. Relapsing polychondritis. Analytical literature review and studies on pathogenesis. Am J Med 1966;41:285–99.
11. Balsa-Criado A, Garcia-Fernandez F, Roldan I. Cardiac involvement in relapsing polychondritis. Int J Cardiol 1987;14:381–3.
12. Esdaile J, Hawkins D, Gold P, Freedman SO, Duguid WP. Vascular involvement in relapsing polychondritis. Can Med Assoc J 1977;116:1019–22.
13. Dalal BI, Wallace AC, Slinger RP. IgA nephropathy in relapsing polychondritis. Pathology 1988;20:85–9.
14. Purcelli FM, Nahum A, Monell C. Relapsing polychondritis with tracheal collapse. Ann Otol Rhinol Laryngol 1962;71:1120–9.
15. Daly JF. Relapsing polychondritis of the larynx and trachea. Arch Otolaryngol 1966;84:124–7.
16. Self J, Hammarsten JF, Lyne B, Peterson DA. Relapsing polychondritis. Arch Intern Med 1967;120:109–12.
17. Mitchell N, Shepard N. Relapsing polychondritis. An electron microscopic study of synovium and articular cartilage. J Bone Joint Surg 1972;54-A:1235–45.
18. Gibson GJ, Davis P. Respiratory complications of relapsing polychondritis. Thorax 1974;29:726–31.
19. Kilman WJ. Narrowing of the airway in relapsing polychondritis. Radiology 1978;126:373–6.
20. Mahindrakar NH, Libman LJ. Relapsing polychondritis. J Laryngol Otol 1970;84:337–42.
21. Dahlqvist A, Lundberg E, Ostberg Y. Hydralazine-induced relapsing polychondritis-like syndrome. Acta Otolaryngol 1983;96:355–9.
22. Mohsenifar Z, Tashkin DP, Carson SA, Bellamy PE. Pulmo-

nary function in patients with relapsing polychondritis. Chest 1982;81:711–7.
23. Mendelson DS, Som PM, Crane R, Cohen BA, Spiera H. Relapsing polychondritis studied by computed tomography. Radiology 1985;157:489–90.
24. Neilly JB, Winter JH, Stevenson RD. Progressive tracheobronchial polychondritis: need for early diagnosis. Thorax 1985;40:78–9.
25. Krell WS, Staats BA, Hyatt RE. Pulmonary function in relapsing polychondritis. Am Rev Respir Dis 1986;133: 1120–3.
26. Rogerson ME, Higgins EM, Godfrey RC. Tracheal stenosis due to relapsing polychondritis in rheumatoid arthritis. Thorax 1987;42:905–6.
27. Crockford MP, Kerr IH. Relapsing polychondritis. Clin Radiol 1988;39:386–90.
28. Davis AD, Berkmen YM, King T. Peripheral bronchial involvement in relapsing polychondritis: demonstration by thin-section CT. AJR 1989;153:953–4.
29. Isaak BL, Liesegang TJ, Michet CJ. Ocular and systemic findings in relapsing polychondritis. Ophthalmology 1986; 93:681–9.
30. Rayl JE. Tracheobronchial collapse during cough. Radiology 1965;85:87–92.
31. Miller RD, Hyatt RE. Obstructing lesions of the larynx and trachea: clinical and physiologic characteristics. Mayo Clin Proc 1969;44:145–61.
32. Fry DL, Hyatt RE. Pulmonary mechanics. A unified analysis of the relationship between pressure, volume and gasflow in the lungs of normal and diseased human subjects. Am J Med 1960;29:672–89.
33. Shim C, Corro P, Park SS, Williams MH. Pulmonary function studies in patients with upper airway obstruction. Am Rev Respir Dis 1972;106:233–8.
34. Miller RD, Hyatt RE. Evaluation of obstructing lesions of the trachea and larynx by flow-volume loops. Am Rev Respir Dis 1973;108:475–81.
35. Foidart J-M, Abe S, Martin GR, et al. Antibodies to type II collagen in relapsing polychondritis. N Engl J Med 1978;299: 1203–7.
36. Rajapakse DA, Bywaters EGL. Cell-mediated immunity to cartilage proteoglycan in relapsing polychondritis. Clin Exp Immunol 1974;16:497–502.
37. Arundell FW, Haserod JR. Familiar chronic atrophic polychondritis. Arch Dermatol 1960;82:439–41.
38. Thomas L. Reversible collapse of rabbit ears after intravenous papain, and prevention of recovery by cortisone. J Exp Med 1956;104:245–52.
39. McCune WJ, Schiller AL, Dynesius-Trentham RA, Trentham DE. Type II collagen-induced auricular chondritis. Arthritis Rheum 1982;25:266–73.
40. Tadaki T, Aiba S, Igarashi M, Tagami H. Analysis of increased urinary acid glycosaminoglycans in a patient with relapsing polychondritis. Acta Derm Venereol (Stockh) 1987; 67:441–5.
41. Svenson KLG, Holmdahl R, Klareskog L, et al. Cyclosporin A treatment in a case of relapsing polychondritis. Scand J Rheumatol 1984;13:329–33.
42. Grillo HC, Zannini P, Michelassi F. Complications of tracheal reconstruction. Incidence, treatment, and prevention. J Thorac Cardiovasc Surg 1986;91:322–8.
43. D'Amico DF, Bassi N, Callegari P, et al. Surgical management of tracheal stenoses: personal experience with 105 cases. Ital J Surg Sci 1987;17:113–6.
44. Montgomery WM. T-tube tracheal stent. Arch Otolaryngol 1965;82:320–1.
45. Neville WE, Bolanowski JP, Kotia GG. Clinical experience with the silicone tracheal prosthesis. J Thorac Cardiovasc Surg 1990;99:604–13.
46. Landa L. The tracheal T-tube in tracheal surgery. In: Grillo HC, Eschapasse H. eds. International trends in general thoracic surgery; vol 2. Philadelphia: W.B. Saunders, 1987: 124–32.
47. Meurala H, Halttanen P, Standerskjold-Nordenstam C-G, Keskitalo E. Surgical support of collapsing intrathoracic tracheomalacia after thyroidectomy. Acta Chir Scand 1982;148: 127–9.
48. Grillo HC. Notes on the windpipe. Ann Thorac Surg 1989; 47:9–26.
49. Herzog H, Heitz M, Keller R, Graedel E. Surgical therapy for expiratory collapse of the trachea and large bronchi. In: Grillo HC, Eschapsse H, eds. International trends in general thoracic surgery; vol 2. Philadelphia: W.B. Saunders, 1987: 74–90.
50. Rainer WG, Hutchinson D, Newby JP, Hamstra R, Durrance J. Major airway collapsibility in the pathogenesis of obstructive emphysema. J Thorac Cardiovasc Surg 1963;46:559–67.
51. Maurer W, Nadjafi A, Keller R, et al. Die chirurgische Behandlung der exspirarotischen Tracheobronchialstenose. Thoraxchirurgie 1968;16:480–6.
52. Halttunen P, Meurala, Standertskjold-Nordenstam C-G. New surgical correction of central airway collapse in an asthmatic patient. Scand J Thorac Cardiovasc Surg 1981;15: 343–5.
53. Halttunen P. EDH-adhesive plastic support in the surgical treatment of tracheobronchial collapse. Acta Chir Scand 1973;(Suppl 440):1–34.
54. Eng J, Sabanathan S. Tissue adhesive in bronchial closure. Ann Thorac Surg 1989;48:683–5.
55. Wiedemann HP, Matthay RA. Pulmonary manifestations of the collagen vascular diseases. Clin Chest Med 1989;10: 677–722.
56. Case records of the Massachusetts General Hospital (Case 50-1985). N Engl J Med 1985;313:1530–7.

CORRESPONDENCE

Nifedipine After Coronary Bypass Grafting
To the Editor:

Seitelberger and associates [1] have concluded from their very interesting study that continuous infusion of nifedipine after elective coronary artery bypass grafting can decrease the incidence of myocardial infarction in the early postoperative period. This information could have an important impact on the care of the many patients undergoing coronary revascularization. I have two concerns (one minor, the other major) regarding this study. First, the minimum nifedipine infusion rate quoted, 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$, is unusually high and would produce plasma levels far in excess of the stated 13 to 29 ng/mL range. Could the rate have been 10 $\mu g \cdot kg^{-1} \cdot h^{-1}$?

Second, 1 of 22 analyzable patients in the nifedipine group was diagnosed as having suffered a myocardial infarction compared with 4 of 23 analyzable control patients (reference 1, table 4). The appropriate statistical analysis is, I believe, a two-tailed Fisher's exact test which gives $p = 0.346$ (the one-tailed gives $p = 0.187$ and an uncorrected χ^2 gives $p = 0.170$). These tests indicate that there is greater than a 5% chance that the findings were due to chance and not to a beneficial effect of nifedipine.

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Reference

1. Seitelberger R, Zwölfer W, Binder TM, et al. Infusion of nifedipine after coronary artery bypass grafting decreases the incidence of early postoperative myocardial ischemia. Ann Thorac Surg 1990;49:61–8.

Aspirin and Blood Loss
To the Editor:

While agreeing that Taggart and associates [1] have demonstrated that even low-dose aspirin leads to increased blood loss and transfusion requirements after coronary artery bypass grafting, we believe that some of their conclusions and recommendations warrant questioning.

Although there is a significant difference in blood loss and transfusion requirements between the control group and the aspirin subgroups, from Figure 1, there would appear to be no obvious intergroup difference as the median and interquartile ranges overlap to such a great extent. This is also borne out by the confidence intervals given in the text for postoperative blood loss and transfusion requirements. The possibility of an aspirin paradox does not therefore arise. This would be consistent with previous studies, including one from our own group [2], demonstrating that even 75 mg of aspirin given 24 hours preoperatively has a very substantial inhibitory effect on saphenous vein prostacyclin production.

In addition, while agreeing that preoperative low-dose aspirin therapy may increase transfusion requirements and the need for haemostatic products after coronary bypass grafting, we would question the recommendation advocated both by them and by Dr Gay in the accompanying editorial [3] regarding discontinuation of aspirin therapy 1 week before operation.

Approximately 20% of saphenous vein grafts suffer thrombotic occlusion during the first 12 months, a substantial proportion of which may do so during the first few hours postoperatively [4]. Aspirin, by its action, minimizes platelet adhesion and activation leading to a greater short-term patency rate [4, 5]. Should we not therefore accept that the increased postoperative blood loss and transfusion requirements associated with aspirin are the price we have to pay for improved graft patency? If we accept this, the question then to be decided is what the optimum time for discontinuation of aspirin therapy preoperatively should be to allow recovery of vascular prostacyclin production while maintaining the benefit of platelet inactivation.

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References

1. Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. Ann Thorac Surg 1990;50:425–8.
2. Angelini GD, Breckenbridge IM. Is there a rationale for treatment with aspirin before coronary surgery? Lancet 1985; 2:843.
3. Gay WA Jr. Aspirin, blood loss, and transfusion. Ann Thorac Surg 1990;50:345.
4. Angelini GD, Newby AC. The future of saphenous vein as a coronary artery bypass conduit. Eur Heart J 1989;10:273–80.
5. Fuster V, Chesebro JH. Aortocoronary artery vein-graft disease: experimental and clinical approach for the understanding of the role of platelets and platelet inhibitors. Circulation 1985;72(Suppl 5):65–70.

Reply
To the Editor:

The possibility of an aspirin paradox with low-dose aspirin [1] referred to the observation that the median increase in postoperative blood loss of 490 mL in the 150-mg-aspirin group was almost double that of the 75-mg and 300-mg groups (280 mL and 230 mL, respectively). While we accept that this difference did not reach statistical significance, this may simply reflect the small numbers of patients in each of the individual aspirin groups and the relatively wide scatter of the data.

Drs Violaris and Angelini question our recommendation of discontinuing aspirin therapy before operation, stating that a "substantial proportion" of vein graft occlusions may occur during the first few postoperative hours. However, the article they cite in apparent support of this statement [2] provides no such evidence, as the earliest time at which angiograms have been performed in patients after coronary artery operations is the eighth postoperative day [3]. The inference that discontinuation of aspirin in the preoperative period may adversely affect short-term patency rates is, again, not supported by either of the references cited [2, 4]. Indeed, a recent study by Goldman and associates [5] demonstrated no difference in angiographically confirmed vein graft patency 1 year after operation whether aspirin was administered 12 hours before or 6 hours after operation.

Our recommendation that aspirin therapy be discontinued 1 week before operation and recommenced 6 hours after operation is based on two observations: (1) the antiplatelet effects of aspirin are apparent within a few hours of administration and persist for at least the subsequent 7 days [6], and (2) cardiopulmonary

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bypass induces qualitative and quantitative deficiences in platelets that persist for at least 6 hours after operation [7].

In view of the well-recognized risks of transmissible infections associated with transfusion of blood products, and in the absence of any evidence of a definite advantage of preoperative as opposed to early postoperative administration of aspirin, we do not accept that "the increased postoperative blood loss and transfusion requirements associated with aspirin are the price we have to pay for improved graft patency." In the light of our own results and those of Goldman and associates, we stand by our recommendation of discontinuing aspirin therapy 1 week before operation and reintroducing it in the very early postoperative period.

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References

1. Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. Ann Thorac Surg 1990;50:425–8.
2. Angelini GD, Newby AC. The future of saphenous vein as a coronary artery bypass conduit. Eur Heart J 1989;10:273–80.
3. Chesebro JH, Fuster V, Elveback LR, et al. Effect of dipyridamole and aspirin on late vein-graft patency after coronary bypass operations. N Engl J Med 1984;310:209–14.
4. Fuster V, Chesebro JH. Aortocoronary artery vein-graft disease: experimental and clinical approach for the understanding of the role of platelets and platelet inhibitors. Circulation 1985;72(Suppl 5):65–70.
5. Goldman S, Copeland J, Mortiz T, et al. Internal mammary artery and saphenous vein graft patency. Effects of aspirin. Circulation 1990;82(Suppl 4):237–42.
6. Amescua JL, O'Grady J, Salmon JA, Moncada S. Prolonged paradoxical effect of aspirin on platelet behaviour and bleeding time in man. Thromb Res 1979;16:69–79.
7. Walker ID, Davidson JF, Faichney A, Wheatley DJ, Davidson KG. A double blind study of prostacyclin in cardiopulmonary bypass surgery. Br J Haematol 1981;49:415–23.

Traumatic Aortic Insufficiency

To the Editor:

We enjoyed reading the paper from Ovil and associates entitled "Aortic valvoplasty for traumatic aortic insufficiency: a 2-year follow-up" [1]. Traumatic aortic insufficiency is a rare occurrence and, as stated in this article, valve replacement is performed in most cases.

We would like to add another case of aortic valvoplasty that we reported in 1985 [2]. A 50-year-old man started to complain of precordial chest pain and shortness of breath on exertion 10 weeks after a violent motorcycle accident. The physical examination showed a grade 4 diastolic murmur; echocardiography revealed aortic cusp prolapse inside the left ventricle. Cardiac catheterization demonstrated massive aortic insufficiency and left ventricular dilatation associated with diffuse hypokinesia.

At operation, a laceration was found in the middle of the noncoronary cusp extending from the edge to the annulus perpendicular to the free edge of the cusp (Fig 1). Valvoplasty was performed by suturing the defect with interrupted 6-0 Prolene sutures. The postoperative course was uneventful and the patient was discharged 2 weeks after operation. This patient has resumed normal professional activity.

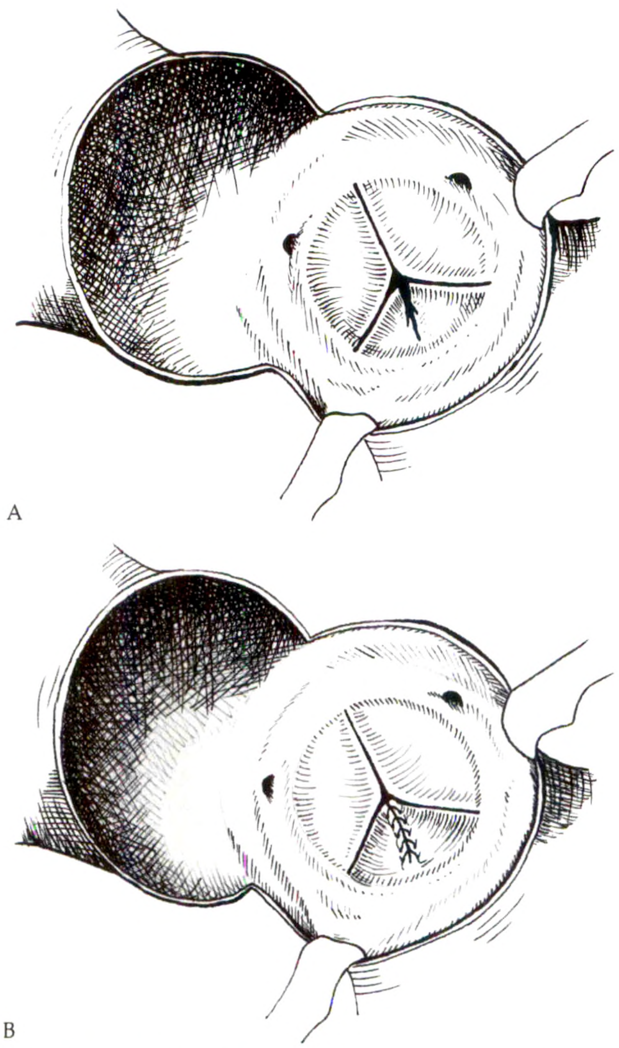

Fig 1. Operative view of the lesion (A) before suturing and (B) after suturing.

Now, 6½ years after, he is still doing very well. Yearly

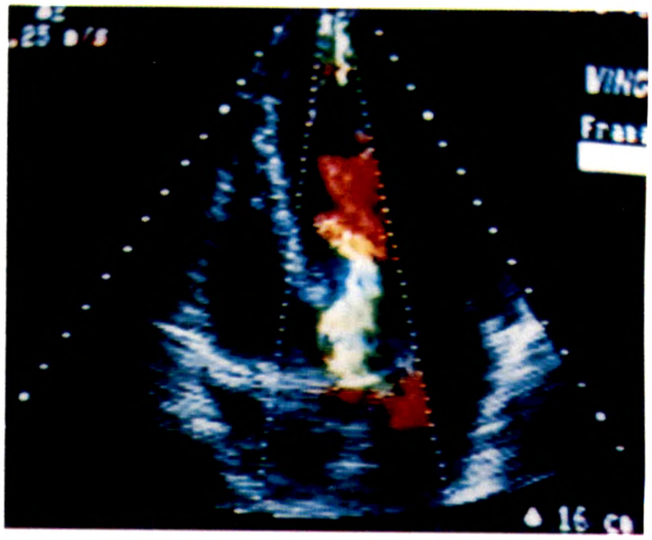

Fig 2. The aortic valve shows minimal incompetence.

echocardiography has shown reduction of the left ventricular cavity (28 mm in systole and 47 mm in diastole) associated with an almost normal aortic valvar function (minimal aortic incompetence is demonstrated in Figure 2).

In that type of clear-cut lesion, aortic valvoplasty is obviously a reliable solution for obtaining good valve function and, in the long run, an optimal quality of life.

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References

1. Ovil Y, Wahi R, Liu P, Goldman B. Aortic valvoplasty for traumatic aortic insufficiency: a 2-year follow-up. Ann Thorac Surg 1990;49:143–4.
2. Grande AM, Vigna V, Bex JP. Valvular injuries resulting from blunt chest trauma. Tex Heart Inst J 1985;12:261–4.

Malignant Fibrous Histiocytoma of the Trachea

To the Editor:

Randleman and associates [1] are to be congratulated for their successful diagnosis and management of an unusual tracheal tumor. However, we would like to point out one aspect of their management we believe may have been in error—the use of preliminary tracheostomy to provide an airway in such a situation is rarely necessary. Airway stenoses, both benign and malignant, can virtually always be dilated with a rigid bronchoscope, permitting adequate ventilation and obviating the need for emergency tracheostomy. In lateral tracheal tumors of the type they reported, a small endotracheal tube can usually be passed next to the tumor along the uninvolved tracheal wall. Dilation with a rigid bronchoscope or occasionally debulking with a biopsy forceps or yttrium-aluminum-garnet laser may be necessary beforehand. Serious bleeding is rarely a problem. Alternatively, the endotracheal tube may be left above the tumor or a small catheter passed beyond it and used for jet ventilation. Placing a tracheostomy in the normal distal trachea may compromise the subsequent resection by reducing the total length of trachea that can be removed safely and should be avoided.

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Reference

1. Randleman CD, Unger ER, Mansour KA. Malignant fibrous histiocytoma of the trachea. Ann Thorac Surg 1990;50:458–9.

Reply

To the Editor:

In response to Drs Streitz and Shapshay, we think there may be a misunderstanding. They stated that *preliminary* tracheostomy to provide an airway in patients with tracheal strictures is rarely necessary, and we are in total agreement. We did not do a *preliminary* tracheostomy either.

We have also dilated tracheal strictures with a rigid bronchoscope, passed small endotracheal tubes through narrowed segments, and ventilated patients with the endotracheal tube left above the stenotic area. However, we have not placed a tracheostomy tube in normal distal trachea as we have been accused of doing. We simply divided the trachea just distal to the tumor and intubated the distal trachea for ventilation (and we called that a tracheostomy!). We then did an end-to-end anastomosis as usual. And accordingly, no preliminary tracheostomy was done.

On a final note, a preliminary tracheostomy, done as a separate procedure, should not be totally condemned, and it should not necessarily be included in a subsequent resection. We recently performed a tracheal resection on a young man who had a severe 2-mm postintubation tracheal stricture when seen in the emergency room of another hospital and who had a tracheostomy performed as a life-saving procedure. The treating physician evidently did the right thing for his level of training and clinical judgment.

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Complement Activation and Lung Permeability During Cardiopulmonary Bypass

To the Editor:

We enjoyed the recent paper by Tennenberg and colleagues [1] in which they report increases in activated complement components and in neutrophil expression of *n*-formyl-methionyl-leucyl-phenylalanine receptors, but no significant changes in lung epithelial permeability. However, their data do not necessarily support the view that complement and neutrophil activation during cardiopulmonary bypass is not associated with acute lung injury.

Cardiopulmonary bypass is well known to cause activation of neutrophils and of the complement system [2–4]; more recently, pulmonary sequestration of neutrophils has been demonstrated with the release of enzymes and the production of lipid peroxides [5]. It has been suggested that activated neutrophils play a central role in the pulmonary damage after bypass [5]. Types of oxygenator that cause greater neutrophil and complement activation tend also to be associated with greater pulmonary impairment [6–8].

The measurement of lung epithelial permeability by technetium 99m–labeled diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) clearance is a less than ideal method of assessing pulmonary damage. Although previous studies by Tennenberg and co-workers [9] suggest that increased ^{99m}Tc-DTPA clearance reflecting increased lung epithelial permeability precedes the clinical manifestations of adult respiratory distress syndrome in patients with sepsis and multiple trauma, others have drawn attention to the limitations of this technique [10, 11]. As Tennenberg and colleagues acknowledge in their Comment, it is conceivable that serious pulmonary vascular and endothelial damage could occur without changes in epithelial permeability. Indeed, they report significant increases in alveolar-arterial oxygen tension gradient and intrapulmonary shunt fraction while ^{99m}Tc-DTPA clearance did not change [1]. The technique of double-isotope scintigraphy provides an index of pulmonary microvascular permeability [12, 13], and our own preliminary data suggest that in some patients this has increased significantly at 4 hours after bypass, presumably reflecting pulmonary endothelial damage.

The lack of a demonstrable change in lung *epithelial* permeability does not necessarily mean that there are no pulmonary changes, nor that these changes would not correlate with indices of complement and neutrophil activation. Instead the apparent lack of change might reflect limitations of the ^{99m}Tc-DTPA clearance technique or the relatively small number of patients in this study. This careful and detailed observations by Tennenberg and colleagues are of great interest, but further studies are required.

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References

1. Tennenberg SD, Clardy CW, Bailey WW, Solomkin JS. Complement activation and lung permeability during cardiopulmonary bypass. Ann Thorac Surg 1990;50:597–601.
2. Riegel W, Spillner G, Schlosser V, Horl WH. Plasma levels of main granulocyte components during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1988;95:1014–9.
3. Hammerschmidt DE, Stroncek DF, Bowers TK, et al. Complement activation and neutropenia occurring during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1981;81:370–7.
4. Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983; 86:845–57.
5. Westaby S. Neutrophil protease enzymes and oxygen free radicals as mediators of pulmonary membrane damage. Progr Clin Biol Res 1987;236A:75–86.
6. Cavarocchi N, Pluth JR, Schaff HV, et al. Complement activation during cardiopulmonary bypass. Comparison of bubble and membrane oxygenators. J Thorac Cardiovasc Surg 1986;91:252–8.
7. Darcy CM, Townsend ER, Boylett A, Chan SL, Parker-Williams J. Pulmonary dysfunction associated with cardiopulmonary bypass: a comparison of bubble and membrane oxygenators. Circulation 1981;64(Suppl 2):54–7.
8. Byrick RJ, Noble WH. Postperfusion lung syndrome. Comparison of Travenol bubble and membrane oxygenators. J Thorac Cardiovasc Surg 1978;76:685–93.
9. Tennenberg SD, Jacobs MP, Solomkin JS. Complement-mediated neutrophil activation in sepsis- and trauma-related adult respiratory distress syndrome: clarification with radioaerosol lung scans. Arch Surg 1987;122:26–32.
10. Cooper JA, Feustel PJ, Line BR, Malik AB. Pulmonary epithelial clearance of ^{99m}Tc-DTPA after thrombin-induced pulmonary microembolism. Am Rev Respir Dis 1986;134: 734–8.
11. Braude S, Nolop KB, Hughes JMB, Barnes PJ, Royston D. Comparison of lung vascular and epithelial parmeability indices in the adult respiratory distress syndrome. Am Rev Respir Dis 1986;133:1002–5.
12. Basran GS, Byrne AJ, Hardy JG. A noninvasive technique for monitoring lung vascular permeability in man. Nucl Med Commun 1985;3:3–10.
13. Keegan J, Bailey J, Wilkinson P, Davies S, Rudd R. Pulmonary microvascular permeability using double isotope scintigraphy. Nucl Med Commun 1989;10:871–8.

Reply

To the Editor:

I appreciate the opportunity of responding to the comments of Davies and associates concerning our recent article [1]. As the article states, I can only contend that complement and neutrophil activation during cardiopulmonary bypass is not associated with acute lung injury in the context of ^{99m}Tc-DTPA radioaerosol-determined pulmonary epithelial permeability. Although, for the purposes of this article, I refer to acute lung injury as defined by changes in pulmonary epithelial permeability, I would argue that clinically significant acute lung injury rarely occurs after cardiopulmonary bypass.

I must admit that my observations in cardiopulmonary bypass are motivated by a greater interest in the adult respiratory distress syndrome and its pathophysiology. I can think of no better clinical experiment for the theory of complement-mediated acute lung injury than cardiopulmonary bypass. One finds astoundingly high levels of activated complement components and easily demonstrable evidence of neutrophil activation, yet clinical acute lung injury is quite rare and, as our study showed, subclinical abnormalities similar to those seen in patients at high risk for the development of adult respiratory distress syndrome are also not evident. It is these observations that continue to shift my interest away from complement activation and toward other mechanisms of cell activation and lung injury.

I look forward to the future work of Davies and colleagues, which will help to define the microvascular changes associated with cardiopulmonary bypass.

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Reference

1. Tennenberg SD, Clardy CW, Bailey WW, Solomkin JS. Complement activation and lung permeability during cardiopulmonary bypass. Ann Thorac Surg 1990;50:597–601.

Gastrotracheal Fistula as a Result of Radiotherapy After Transhiatal Esophagectomy

To the Editor:

One of the rare complications of transhiatal esophagectomy is membranous tracheal injury. But it is also demonstrated by Kron and associates [1] that gastrotracheal fistula can be seen as a late complication after transhiatal esophagectomy. We present a case of gastrotracheal fistula after transhiatal esophagectomy and radiotherapy.

The patient is a 55-year-old man with a history of dysphagia. His esophagogram revealed a 4-cm segment of narrowing in the lower third of esophagus. After esophagoscopy, the histopathological diagnosis was spinocellular cancer. He underwent a transhiatal esophagectomy with gastric pull-up in April 1988. The suture technique, but no stapler, was used for anastomosis. He was discharged from the hospital 10 days after this operation and has had no problems.

The patient had six courses of chemotherapy (Adriamycin, vincristine, cisplatin) in our hospital. Ten months after operation, he was treated at a radiotherapy center in Ankara; irradiation of the mediastinum (40 Gy) was carried out. He did well for 6 months and then had cough and hemoptysis. He underwent bronchoscopy and esophagoscopy in December 1989 and was diagnosed as having gastrotracheal fistula. There was no recurrence of tumor around the fistula as confirmed by histopathological examination. The patient was operated on for fistula repair. He underwent a right thoracotomy and fistula repair as described by Kron and associates [1].

The fistula was 1.5 × 2 cm at the membranous trachea just above the tracheal bifurcation. The fistula was dissected and the tracheal membranous defect was closed with a 3-cm portion of pericardium with a running 3-0 Prolene suture. A pleural flap also was used to cover the pericardial closure. The opening of the stomach was oversewn with two-layer closure. A latissimus dorsi flap was interposed between the tracheal and gastric suture lines. In his postoperative course, aplastic anemia developed as a result of Metamisole administration. The patient died of bilateral pneumonia and sepsis.

Transhiatal esophagectomy is a preferred method because of a low rate of morbidity and mortality [2, 3]. Kron and associates [1] reported a gastrotracheal fistula as a late complication after transhiatal esophagectomy. This is the result of stapler application. In our case the cause of fistula was radiotherapy. Stomach is more sensitive to radiotherapy than esophagus. The dose of this therapy should be managed carefully. As seen from this report, 40 Gy of radiotherapy can cause such a fistula. No recurrence was detected around the fistula histopathologically. This also confirms that the fistula was not caused by tumor infiltration.

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References

1. Kron IL, Johnson AM, Morgan RF. Gastrotracheal fistula: a late complication after transhiatal esophagectomy. Ann Thorac Surg 1989;47:767–8.
2. Orringer MB. Transthoracic versus transhiatal esophagectomy: what difference does it make? Ann Thorac Surg 1987; 44:116–8.
3. Hankins JR, Attar S, Coughlin TR Jr, et al. Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg 1989;47:700–5.

Reply

To the Editor:

I read with interest the case described by Dr Paç and associates. Clearly in their case, radiation therapy played a role in this fistula. This case also serves to support our contention that benign gastric gastrotracheal fistula can occur after esophagectomy owing to multiple causes. One should not develop a pessimistic response and assume carcinoma in these cases of late gastrotracheal fistula.

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Circulatory Support 1991

The Second International Conference on Circulatory Support Devices in End-Stage Heart Disease

San Francisco Marriott Hotel, San Francisco, California
November 15–17, 1991 (weekend meeting)

Circulatory Support 1991 will be a comprehensive multidisciplinary meeting focusing on the clinical applications of the entire spectrum of circulatory support devices. Surgeons, cardiologists, anesthesiologists, intensivists, perfusionists, engineers, and operating room and intensive care nurses are encouraged to attend as individuals or as a team.

The meeting is sponsored by The Society of Thoracic Surgeons under the direction of its Committee on Circulatory Assist Devices and Artificial Hearts. Committee members are: D. Glenn Pennington, MD, Chairman; Jack G. Copeland, MD; Charles Hahn, MD; J. Donald Hill, MD; George J. Magovern, MD; Peer M. Portner, PhD; and Glenn Rahmoeller.

For this weekend meeting, the Saturday morning segment entitled "Problem Cases" will include panel and audience discussions of four major subject areas: patient selection; anticoagulation management, bleeding, and thromboembolic risk; infections—prophylaxes and treatment; and management of secondary organ dysfunction. An outstanding international panel has been chosen to represent a broad spectrum of opinions for each subject.

Late Saturday morning and early afternoon, video sessions on the working details and proposed indications for support devices that are currently in use or development will be presented. A report of the current circulatory support device registry will be given. Breakout sessions of smaller groups will follow and focus on how to use external nonpulsatile circulatory support, external pulsatile circulatory support, and internal pulsatile circulatory support.

The Sunday sessions from 7:45 AM to 1:00 PM will be devoted to state-of-the-art presentations covering: emergency resuscitation techniques, heparinless bypass, the Hemopump experience, postoperative use of the Biopump, the VAD experience in Japan, optimizing hemodynamics and assessing myocardial recovery, right heart management during LVAD support, circulatory support in children, bridge to transplantation with the Thoratec VAD and with the Symbion TAH, chronic support with the TCI left ventricular assist system, the Novacor left ventricular assist system, and the Penn State TAH.

Poster presentations concerning a wide variety of subjects related to circulatory support as well as commercial exhibits demonstrating currently available devices will be available during breaks. Full CME credit will be provided for attendees.

The deadline for submission of poster abstracts is August 1, 1991. For further information and guidelines on poster abstract submission and other available meeting information, contact: The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; telephone: (312) 644-6610.

PROGRAM

Saturday, November 16

8:00–8:15 Welcome and Opening Remarks

Problem Case-Oriented Panels

8:15–8:55 **Panel I: Patient Selection**
Moderator: D. Glenn Pennington, St. Louis, MO

Panelists: David J. Farrar, San Francisco, CA; Daniel Loisance, Paris, France; Walter E. Pae, Jr, Hershey, PA; and Robert W. Emery, Minneapolis, MN

8:55–9:15 **Registry Report**
Walter E. Pae, Jr, Hershey, PA

9:15–10:05 **Video Session I**
Discussion Leader: W. Gerald Rainer, Denver, CO

10:05–10:50 **Break to Visit Posters/Exhibits**

10:50–11:40 **Video Session II**
Discussion Leader: Wilbert J. Keon, Ottawa, Canada

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11:40–12:30 **Video Session III**
Discussion Leader: Ernst Wolner, Vienna, Austria

12:30–1:30 **Lunch**

1:40–2:40 **"How To" Panel Session I**

1. Nonpulsatile Circulatory Support
   Moderator: George J. Magovern, Pittsburgh, PA

   Panelists: Richard K. Wampler, Rancho Cordova, CA; Leonard A. R. Golding, Cleveland, OH; and Lyle D. Joyce, Minneapolis, MN
2. External Pulsatile Circulatory Support
   Moderator: J. Donald Hill, San Francisco, CA

   Panelists: Y. Sezai, Tokyo, Japan; Roland Hetzer, Berlin, Germany; and Robert A. Guyton, Atlanta, GA
3. Internal Pulsatile Circulatory Support
   Moderator: Peer M. Portner, Oakland, CA

   Panelists: William A. Baumgartner, Baltimore, MD; Christian Cabrol, Paris, France; and O. Howard Frazier, Houston, TX

2:45–3:45 **"How To" Panel Session II**

1. Nonpulsatile Circulatory Support
   Moderator: George Paul Noon, Houston, TX

   Panelists: Jack J. Curtis, Columbia, MO; Charles Henry Moore III, San Antonio, TX; and Michael S. Sweeney, Houston, TX
2. External Pulsatile Circulatory Support
   Moderator: Charles-Julien Hahn, Arzier, Switzerland

   Panelists: William L. Holman, Birmingham, AL; Jack G. Copeland III, Tuscon, AZ; and Gerard Champsaur, Lyon, France
3. Internal Pulsatile Circulatory Support
   Moderator: Philip E. Oyer, Stanford, CA

   Panelists: John M. Armitage, Pittsburgh, PA; Terence Lewis, London, England; and Roque P. Pifarre, Chicago, IL

3:45–4:30 **Break**
Visit Posters and Exhibits

4:40–5:10 **Panel II: Anticoagulation**
Moderator: Jack G. Copeland III, Tucson, AZ

Panelists: O. Howard Frazier, Houston, TX; Lawrence R. McBride, St. Louis, MO; Marko Turina, Zurich, Switzerland; and Christian Cabrol, Paris, France

5:10–5:50 **Panel III: Infections—Prophylaxis and Treatment**
Moderator: J. Donald Hill, San Francisco, CA

Panelists: Bartley P. Griffith, Pittsburgh, PA; Charles-Julien Hahn, Arzier, Switzerland; and Paul Didisheim, Bethesda, MD

5:50–6:30 **Panel IV: Management of Secondary Organ Dysfunction**
Moderator: William S. Pierce, Hershey, PA

Panelists: James J. Hershon, San Francisco, CA; Robert L. Kormos, Pittsburgh, PA; Walter P. Dembitsky, San Diego, CA; and George Paul Noon, Houston, TX

Sunday, November 17

6:40–7:40 **Special Breakfast Panel V: Long-Term Biventricular**
Moderator: Charles-Julien Hahn, Arzier, Switzerland

Panelists: William S. Pierce, Hershey, PA; Donald Olson, Salt Lake City, UT; Kenneth Butler, Rancho Cordova, CA; David Lederman, Danvers, MA; and John Wallwork, Cambridge, England

7:45–9:20 **State of the Art I**
Moderator: Frank C. Spencer, New York, NY

1. Emergency Resuscitation With ECMO
   Walter P. Dembitsky, San Diego, CA
2. Circulatory Support With Heparinless CPB
   Per Olsson, Stockholm, Sweden
3. Hemopump Clinical Results and Applications
   Richard K. Wampler, Rancho Cordova, CA
4. Biopump in Postoperative Circulatory Support
   George J. Magovern, Pittsburgh, PA
5. VAD Experience (Postcardiotomy and AMI) in Japan
   Hisateru Takano, Osaka, Japan

9:20–10:05 **Break**

10:05–11:25 **State of the Art II**
Moderator: Michael E. DeBakey, Houston, TX

6. Optimizing Hemodynamics and Assessing Myocardial Recovery
   George Paul Noon, Houston, TX
7. Right Heart Management During LVAD Use
   Bartley P. Griffith, Pittsburgh, PA
8. Status of Circulatory Support in Children
   D. Glenn Pennington, St. Louis, MO
9. To be announced

11:25–1:00 **State of the Art III**
Moderator: Norman E. Shumway, Stanford, CA

10. Bridge to Transplant With the Thoratec VAD
    J. Donald Hill, San Francisco, CA
11. Bridge to Transplant With the Symbion J7 TAH
    Christian Cabrol, Paris, France
12. Chronic Support With the TCI LVAS
    O. Howard Frazier, Houston, TX
13. Chronic Support With the Novacor LVAS
    Peer M. Portner, Oakland, CA
14. Lessons From Intermediate Support That Will Implement Permanent Support
    William S. Pierce, Hershey, PA

Southern Thoracic Surgical Association Rules for Submission of Abstracts

Abstracts for papers to be presented for the 1991 Annual Meeting are now being accepted. The deadline for postmark of abstracts is May 15, 1991. An original and 1 copy should be submitted, using the official Association abstract form, to Frederick L. Grover, MD, Chairman, Program Committee, The Southern Thoracic Surgical Association, 401 North Michigan Ave, Chicago, IL 60611-4267. Additional forms are available upon request from the Association.

Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. *Abstracts received after the deadline will not be considered.* The information requested at the bottom of this form must be completed indicating who is to receive the notice of acceptance or rejection and who will present the paper if accepted.

Abstracts may be submitted for the regular program, the Forum, or either. Papers selected for the Forum will be published in *The Annals of Thoracic Surgery* if they pass the usual editorial review.

Essayists are reminded that all papers accepted for presentation must be submitted in triplicate to Hendrick B. Barner, MD, Secretary-Treasurer, at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation.

Abstracts frequently obscure the value of their content because they are poorly organized. It is important that methods and results be clearly defined in the abstract; general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Presentations in the regular program are limited to 10 minutes; those in the Forum are limited to 5 minutes.

In discussion of papers, the Association encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of the discussion in the form of "secondary papers" will not be welcomed.

INSTRUCTIONS FOR ABSTRACTS

The official abstract form or photocopies must be used. **Authors must indicate whether they want the abstract considered for the regular program, the Forum, or either by checking the appropriate box. Authors must also categorize the principal subject of their abstract by checking the appropriate box.**

1. Title of abstract must be completely CAPITALIZED.
2. Full names of authors must appear on the abstract, without degrees, titles, or appointments.
3. Indicate each author who is a member of the Southern Thoracic Surgical Association with an asterisk following the name.
4. Underline the name of each STSA new member (elected to membership in 1990).
5. Institution or address is to be given.
6. Abstracts must be limited to 200 words and *must be typed double-spaced.*
7. When percentages are used, the absolute numbers of derivation must be stated.
8. The body of the abstract should include:
   a. A brief statement of the purpose of the study, referring, as appropriate, to the current state of research in the field.
   b. The methods of study or experimental approach clearly defined.
   c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
   d. A statement concerning the significance and implications of the work.
9. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

THE FOLLOWING INFORMATION MUST BE COMPLETED:

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( ) STSA Member ( ) STSA New Member (1990) ( ) Non-Member

Address correspondence to: ______________________ Telephone: ( ) __________

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OFFICIAL ABSTRACT FORM
SOUTHERN THORACIC SURGICAL ASSOCIATION

Frederick L. Grover, MD
Chairman, Program Committee
Southern Thoracic Surgical Association
401 North Michigan Avenue
Chicago, IL 60611-4267

DEADLINE FOR ABSTRACTS: MAY 15, 1991

For committee use only

Program Number ☐

Abstract Number ☐

Rating (Highest - 10)

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PLEASE READ THE INSTRUCTIONS ON THE OTHER SIDE OF THIS PAGE BEFORE COMPLETING THIS FORM.

I am submitting this abstract for:

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☐ Forum
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Authors:
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Abstract Content
(Indicate one in each category)

Subject

—— Pulmonary
—— Esophagus
—— Chest wall, pleura, and mediastinum
—— Trauma
—— Transplantation
—— Acquired valve disease
—— Coronary artery disease
—— Great vessels
—— Congenital heart and pediatric thoracic
—— Pacemaker and electrophysiology
—— Myocardial protection
—— Extracorporeal circulation and blood coagulation
—— Pulmonary support
—— Endoscopy
—— Other

Scope

—— Clinical
—— Laboratory

COMPLETE THE INFORMATION ON THE OTHER SIDE OF THIS FORM WITH REFERENCE TO THE AUTHOR WHO WILL PRESENT THE PAPER.

I acknowledge that the material will not be presented elsewhere if accepted for presentation on the Southern Thoracic Surgical Association Scientific Program. I further understand that the Editorial Board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

Signature of Senior Author

THE
ANNALS OF
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and the Southern Thoracic Surgical Association*

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

Second Scientific Meeting of the International Association for Cardiac Biological Implants, Washington, DC—May 5, 1991

The topic of this meeting, dedicated in memory of the late Donald Magilligan, MD, will be infective endocarditis of heart valves. For information on this meeting, contact Dr Shlomo Gabbay, Office of the Secretary, UMDNJ, Department of Surgery, Room G502, 100 Bergen St, Newark, NJ 07103.

Seventy-first Annual Meeting of The American Association for Thoracic Surgery, Washington, DC—May 6–8, 1991

For information on this meeting, contact American Association for Thoracic Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Thoracic Imaging 1991, Toronto, Canada—May 13–17, 1991

This meeting is sponsored by The Society of Thoracic Radiology. For information on this meeting, contact Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, GA 30077-1925; or telephone (404) 641-9773 (facsimile: (404) 552-9859).

Surgery for Coronary Artery Disease, Durham, North Carolina—May 20–21, 1991

For information on this meeting, contact Vanessa Moore, PO Box 2986, Duke University Medical Center, Durham, NC 27710, or telephone (919) 684-6077; or contact American College of Cardiology, Extramural Programs Department, 9111 Old Georgetown Rd, Bethesda, MD 20814, or telephone (800) 253-4636.

Fifth International Symposium on Cardiac Bioprostheses, Avignon, France—May 24–27, 1991

This meeting is sponsored by the Scientific Committee for the Advancement of Cardiac Bioprostheses. For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870.

Fourth International Symposium on Echocardiography and Doppler in Cardiac Surgery, Innsbruck, Austria—May 27–29, 1991

For information on this meeting, contact G. Maurer, MD, or W. Mohl, MD, PhD, c/o Interconvention, A-1450 Vienna, Austria; or telephone +43/1/23 69/2642 (telex: 11 18 03; facsimile: +43/1/23 69/648).

Ninth World Symposium on Cardiac Pacing and Electrophysiology, Washington, DC—May 28–31, 1991

This meeting will incorporate the Twelfth Annual Scientific Session of the North American Society of Pacing and Electrophysiology. For information on this meeting, contact IXth World Symposium Secretariat, c/o NASPE, 377J Elliot St, Newton Upper Falls, MA 02164; or telephone (617) 237-1866 (facsimile: (617) 431-1991).

Coronary Artery Surgery and Esophagus Cancer in ARGE ALP and PENTAGONALE, Salzburg, Austria—May 30–June 1, 1991

For information on this meeting, contact Prof Dr Felix Unger or Prof Dr Peter Brücke, c/o Interconvention, Austria Center, Vienna A-1450, Austria; or telephone 43/1/23 69/26 43 (facsimile: 43/1/23 69/648).

The International Society for Cardiovascular Surgery/The Society for Vascular Surgery, Boston, Massachusetts—June 3–5, 1991

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Warm Heart Surgery: Theory, Concepts and Practice, Toronto, Ontario, Canada—June 20, 1991

For information on this meeting, contact Continuing Education, Faculty of Medicine, University of Toronto, Medical Sciences Building, Toronto, Ont M58 1A8, Canada; or telephone (416) 978-2718.

Seventeenth Annual Meeting of The Western Thoracic Surgical Association, Seattle, Washington—June 26–29, 1991

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Second International Seminar on Transplantation for End-Stage Lung Disease, Zurich, Switzerland—June 27–28, 1991

For information on this meeting, contact A.K.M. Congress Service, Clarastrasse 57, Ch 4005 Basel, Switzerland; or telephone 061-691-8888 (facsimile: 061-691-8189).

Techniques in Pulmonary and Oesophageal Surgery, Liverpool, England—July 14–16, 1991

For information on this meeting, contact Mr R. J. Donnelly, The Cardiothoracic Centre, Broadgreen Hospital, Thomas Dr, Liverpool L14 3LB, England; or telephone 051 228 4878 (facsimile: 051 220 8573).

Twentieth World Congress of The International Society for Cardiovascular Surgery, Amsterdam, the Netherlands—September 1–6, 1991

For information on this meeting, contact the Registrar: XX World Congress—ISCVS, International Travel Service, Inc, 104 Wilmot Rd, Suite 300, PO Box 825, Deerfield, IL 60015; or telephone (708) 940-2100 (facsimile: (708) 940-2386); or contact the Congress Secretariat, International Society for Cardiovascular Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Current Issues in Thoracic Organ Transplantation, Essen, Germany—September 19–21, 1991

For information on this meeting, contact Organizing Secretariat, Gisa Brodde Meetings, Saalbau Essen, PO Box 100301, D-4300 Essen 1, Germany; or telephone (0)201-232121 (facsimile: (0)201-232273).

Heart Valve Replacement—Past Performance: Future Prospects, Sheffield, United Kingdom—September 19–21, 1991

For information on this meeting, contact Jenny Pupius, Symposium Secretariat, Department of Medical Physics and Clinical Engineering, Royal Hallamshire Hospital, Glossop Rd, Sheffield S10 2JF, United Kingdom; or telephone (0742) 555250 (facsimile: (0742) 729981).

Fifth Annual Meeting, European Association for Cardio-Thoracic Surgery, London, United Kingdom—September 22–25, 1991

For information on this meeting, contact Organising Secretariat, Conference Associates & Services, Ltd, Congress House, 55 New Cavendish St, London W1M 7RE United Kingdom; or telephone 071 486 0531 (facsimile: 071 935 7559; telex: 934 346 CONFAS G).

Fifth Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery, Alexandria, Egypt—September 23–27, 1991

For information on this meeting, contact Prof M. El-Fiky, Chairman, Cardiac Surgery Department, Ain Shams Faculty of Medicine, Abbassia, Cairo, Egypt; or telephone (202) 834981 or (202) 835495 (facsimile: (202) 834981).

American College of Surgeons, Chicago, Illinois—October 20–25, 1991

For information on this meeting, contact American College of Surgeons, 55 Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-seventh Annual Scientific Assembly, American College of Chest Physicians, San Francisco, California—November 4–8, 1991

For information on this meeting, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, Florida—November 7–9, 1991

For information on this meeting, contact Hendrick B. Barner, MD, Southern Thoracic Surgical Association, 401 N Michigan Ave, Chicago, IL 60611-4267; or telephone (312) 644-6610 (facsimile: (312) 321-6869).

Third Combined Meeting of the Nederlandse Vereniging Voor Thoraxchirurgie and the Deutsche Gesellschaft für Thorax-, Herz- und Gefäßchirurgie, Maastricht, the Netherlands—November 7–9, 1991

For information on this meeting, contact Organizing Secretariat, Conference Agency Limburg, Mrs Brigitte Bessems, c/o University Hospital Maastricht, PO Box 1918, 6201 BX Maastricht, the Netherlands; or telephone 31 (0)43 258344 (facsimile: 31 (0)43 258355).

CLASSIFIED ADS

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Arthur Carlucci, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010 (telephone: (212) 633-3806; facsimile: (212) 633-3880). All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.25 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $17.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad orders should be for a maximum of 6 months; ads may be renewed for up to 6 months at a time. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3853). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the ad. To respond to an anonymous ad, write to Box Number, *The Annals of Thoracic Surgery*, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Thoracic/vascular surgeon needed to join prominent, active 3-man group in desirable suburban community in greater NY metropolitan area. Excellent opportunity for well-trained, highly motivated individual. Recent graduate preferred. Possible academic affiliation. Please respond with CV.

Please respond to Box 404. 404D/I

Cardiac surgeon wanted to join established private practice in upstate New York, primarily adult cardiac. Board certified or eligible required. New or recent graduate preferred. Please send CV and references.

Please respond to M. A. Marvasti, MD, 101 Union Ave, #813, Syracuse, NY 13203. 429K/D

Wanted: BE/BC general surgeon with interest and experience in thoracic surgery who enjoys general surgery, or non-cardiac thoracic surgery, to assume practice of retiring double-boarded thoracic/general surgeon. 34-member multispecialty group in dynamic area hub city of 35,000, with six satellite offices in strategic locations and referral area of 300,000 plus. Superb hospital facilities, including CT, MRI, cardiac surgery, neurosurgery, etc. Directed towards those concerned about quality family lifestyle and professional concerns.

Contact Recruitment Coordinator, Park Clinic, 890 North Eisenhower Ave, Mason City, IA 50401; or dial 800-798-4321 for more information. 431K/D

BC/BE adult cardiothoracic surgeon wanted to join active established department in large multispecialty group practice located in metropolitan Midwest community. Medical school affiliation available. Respond with curriculum vitae.

Please respond to Box 437. 437K/D

Minneapolis cardiothoracic/vascular group seeks to add fifth surgeon, BC/BE.

Respond to BLH Physician Search, 2231 Lee Ave N, Minneapolis, MN 55422; (612) 588-1116 or -0333. 438L/E

Board certified/eligible cardiothoracic surgeon for busy 1-physician practice in Atlanta. Transplant experience. Future partnership.

Send resume to Georgia Cardiac Surgical Association, PO Box 491203, College Park, GA 30349. 439L/E

Cardiovascular and thoracic surgeon, BE/BC, to join another physician in a rapidly expanding private practice located in the Southeast. Please send curriculum vitae and references.

Please respond to Box 459. 459L/E

University of Massachusetts Medical Center is recruiting candidates for its newly opened Cardiothoracic Surgical Residency Program for 1991, 1992, and 1993. The applications for the 1993 position will be processed through the Match Program for Cardiothoracic Residencies.

Request applications from and submit curriculum vitae and three letters of recommendation to Thomas J. Vander Salm, MD, Chief, Division of Cardiothoracic Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655; telephone: (508) 856-2216. 462L/E

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in Dallas. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Respond to Practice Enhancement Resources, PO Box 655999, Dallas, TX 75265; Attention: Carol. 487B/D

Cardiovascular and thoracic surgeon to join established 3-man private practice in mid-South. Practice includes thoracic, cardiac, and vascular surgery. Must be board certified or eligible in thoracic and cardiovascular surgery. Prefer candidate who has recently completed his/her training. Please respond with curriculum vitae.

Please respond to Box 489. 489B/G

A busy greater Boston cardiothoracic surgical group seeks to add a third surgeon as soon as possible. This practice operates from a multihospital referral base. Candidate must be BE/BC. Excellent salary and benefit package. Please respond with CV.

Please respond to Box 490. 490B/D

Cardiovascular/thoracic surgeon wanted to join principal in metropolitan city on west coast of Florida. Must be ABTS certified or eligible and hold Florida license. Good opportunity for young, aggressive, energetic individual. Experience in cardiac transplantation an asset.

Please respond to Box 491. 491B,D,F

Cardiothoracic surgeon, BE/BC, wanted to join 2 surgeons in busy and expanding practice on the West Coast. Experience or training in adult cardiac surgery, thoracic surgery, pacemaker surgery, valve repair, and arrhythmia surgery necessary. Position available July 1991; new or recent graduate preferred. Excellent salary and benefits with eventual partnership possible. Send curriculum vitae and references.

Please respond to Box 497. 497C/E

Cardiovascular surgeon wanted to join a 2-man group in an established practice in the Southeast. Would prefer a recent graduate, but all applications considered. Generous salary leading to partnership. Practice includes all aspects of adult cardiac, thoracic, and vascular surgery. Send curriculum vitae with experience and recommendations.

Please respond to Box 502. 502C/E

Cardiothoracic surgeon to join group of two, in Michigan. Please respond with CV and references.

Please respond to Box 504. 504C/H

Thoracic surgeon, BC/BE, needed to join two others in a busy thoracic surgical practice without open heart surgery. Located in a prime suburb of NYC with a good quality of life. Rapid partnership advancement. Recent graduate preferred. Please reply with a curriculum vitae.

Please respond to Box 505. 505C/D

Cardiothoracic surgeon—second surgeon needed for 200 pump adult cardiac surgery practice in Rocky Mountain region. Salary plus bonus leading to partnership after third year. Send curriculum vitae and references.

Please respond to Box 507. 507C/D

Cardiac surgeon with 3 to 5 years experience in adult cardiac surgery wanted for immediate opening in Northeast. Program now doing 30 to 40 cases/month and senior surgeon needs an experienced #2 individual for long-term commitment. Excellent salary leading to partnership. Reply with curriculum vitae.

Please respond to Box 508. 508C/E

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to Box 509. 509C/H

General thoracic surgeon: the Department of Surgery and the Section of Thoracic Surgery invite applications and nominations for a faculty position in general thoracic surgery at the Assistant or Associate Professor level at the University of Chicago. Prospective candidates should be American Board of Thoracic Surgery eligible or qualified as of July 1, 1991, have demonstrated excellence in clinical surgery and research, and possess a commitment to teaching. Preference will be given to those who have broad experience in general thoracic surgery, including lung transplantation. The successful candidate is expected to develop his/her own research program.

Applicants should have their curriculum vitae and two letters of recommendation sent to Dr Mark Ferguson, Chief, Section of Thoracic Surgery, The University of Chicago, Box 255, 5841 Maryland, Chicago, IL 60637; facsimile: (312) 702-5909. Applications must be received by June 1, 1991. The University of Chicago and its Medical Center are affirmative action/equal opportunity employers. 510C/E

Cardiovascular surgeon to join a young diplomate, ABTS, in a practice that has grown to some 600 hospital surgeries per year. Location is in a city in the mid-South. The only open heart program in 15 counties. 325-bed regional medical center, 2 catherization labs. Practice consists of cardiac, thoracic, and vascular surgery. Full financial support including productivity incentive. All benefits, malpractice and office expenses provided.

Please respond to Box 511. 511C/D

Cardiovascular surgeon: we are looking for a recently trained B/E or B/C CV surgeon to join our very busy and enjoyable 2-man Cardiovascular Department at Billings Clinic, a progressive major regional multispecialty clinic in the northern Rocky Mountain region. This is an outstanding practice opportunity for the right individual seeking a challenging and rewarding surgical practice in surroundings conducive to the highest quality of living for the surgeon and his or her family.

For further information, please call (406) 256-4766 or forward CV to Ann B. Oglesby, MD, MDA, Medical Director, Billings Clinic, PO Box 35100, Billings, MT 59107-5100. 512C/E

Academic institution with private hospital affiliation seeks recent graduate who is board certified or board eligible ABTS for a clinical position as a cardiothoracic surgeon. Applicant should have an interest and expertise in pulmonary and cardiac transplantation as well as teaching.

Please send curriculum vitae to Tom D. Ivey, MD, Department 0251, Cincinnati, OH 45263. 515C/D

Academic cardiothoracic surgeon: the Division of Cardiothoracic Surgery at the University of Massachusetts is expanding its academic faculty. Candidates will be expected to have an interest in developing an active cardiothoracic practice, to participate in thoracic and general surgical residency training, and to take part in clinical and/or laboratory research. The University of Massachusetts is an equal opportunity employer.

Please respond with curriculum vitae to Thomas J. Vander Salm, MD, University of Massachusetts Medical Center, 55 Lake Ave, North, Worcester, MA 01655. 516C/E

Faculty position as associate professor of cardiothoracic surgery, skilled in clinical care of general thoracic surgical patients and experienced in lung transplantation. Must be interested in teaching and laboratory research and able to develop a research program with extramural funding. Send curriculum vitae, bibliography, and three letters of recommendation. The University of Pennsylvania is an equal opportunity/affirmative action employer.

Please respond to Box 518. 518D

Cardiovascular and thoracic surgeon, BC/BE, recently trained, to join an established 3-man private practice group in Southeastern coastal capital city and two-university town. Great hunting, fishing, and sports. Submit CV and references.

Please respond to Box 519. 519D/I

Cardiac surgeon, ABTS eligible/certified. Position available immediately to join established 4-surgeon group practicing adult cardiac surgery. Excellent opportunity for new or recent grad. Practice located in Reading, PA (southeast PA within easy distance of New York and Philadelphia). Guaranteed starting salary and excellent benefits.

Send CV and references to Ashworth and Gregory MDs, 1235 Penn Ave, Wyomissing, PA 19610; (215) 374-5000. 520D/F

Pediatric cardiac surgeon to assume responsibility for established (120 cases per year) and growing pediatric cardiac program as of July 1, 1991.

Address correspondence to Neil R. Thomford, MD, Professor and Chairman, Department of Surgery, Medical College of Ohio, PO Box 10008, Toledo, OH 43699-0008. 522D/G

Division seeks Head of Section of Thoracic Surgery at the University of Washington. Responsible for the academic, educational, and clinical programs including lung transplant program at the University of Washington, Harborview Medical Center, and Seattle Veterans Administration Medical Centers in Seattle. Must be an academician with strong leadership skills, broad clinical experience, documented educational commitment, and a clinical or basic science research record. Faculty level and salary commensurate with experience. University of Washington is an equal opportunity/affirmative action employer.

Please send curriculum vitae to Edward D. Verrier, MD, Chief, Division of Cardiothoracic Surgery, Department of Surgery RF-25, University of Washington, Seattle, WA 98195. 523D

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Please call and/or send CV to Dr John Hutchinson, Chief, Cardiac Surgery, Hackensack Medical Center, 30 Prospect Ave, Hackensack, NJ 07601; telephone: (201) 441-2284 (facsimile: (201) 489-7152). We are a smoke-free facility and a member of University Health System of New Jersey. An equal opportunity employer. 524D

Noncardiac thoracic surgeon—due to retirement, The Mary Imogene Bassett Hospital is seeking a general/thoracic surgeon. MIBH is a multispecialty group practice with a surgical residency and research opportunities. Excellent lifestyle and recreation. Academic appointment at Columbia University.

Contact Michael S. Gold, MD, Surgeon-in-Chief, One Atwell Rd, Cooperstown, NY 13326; (607) 547-3968. 525D/E

Thoracic surgeon—Boston, Massachusetts—currently seeking a board-certified thoracic surgeon to join an existing hospital-based group practice. Carney Hospital is a 382-bed teaching facility with a surgical teaching affiliation with Boston University School of Medicine. The hospital is offering: 3-year guaranteed salary; malpractice insurance; health, life, and long-term disability insurance; 4 weeks paid vacation; paid continuing medical education; fully staffed office.

Interested applicants should forward CV to Lester P. Schindel, Senior Vice President, Corporate Development, Carney Hospital, 2100 Dorchester Ave, Boston, MA 02124. 526D

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Please respond to Box 521. 521D/F

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Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite 312, Sacramento, CA 95819. 480A/F

A 2-year Cardiovascular Research Fellowship position is available 7/1/91 in the Division of Cardiothoracic Surgery at the University of Massachusetts Medical Center. This is an opportunity for a closely supervised and highly productive cardiac research experience. Requirements: (1) A minimum of 2 years of surgical training; (2) a commitment from an institution to complete the applicant's training in general surgery; (3) intentions to pursue an academic career in cardiothoracic surgery.

Interested candidates should contact Marc S. Visner, MD, Division of Cardiothoracic Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655; telephone: (508) 856-2975. 461L/E

Cardiac surgical fellowship at Baystate Medical Center, Springfield, Massachusetts: 2-year appointment beginning July 1, 1991. Salary commensurate with training and consistent with hospital scale. One year intensive exposure and experience opportunity in adult cardiac surgery and 1 year intensive research exposure in myocardial ischemia and preservation. PG-5 or beyond. Interview and references required.

For more information please write Richard M. Engelman, MD, Chief, Cardiac Surgery, Baystate Medical Center, Springfield, MA 01199. 498C/D

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Please contact M. Terry McEnany, MD, Kaiser Foundation Hospital, 2350 Geary Blvd, San Francisco, CA 94115; (415) 929-5499. 513C/H

Fellowship in cardiothoracic and vascular surgery available July 1, 1991. Program includes over 400 open heart surgery cases and 200 thoracic or vascular procedures. New Jersey medical license required. Good salary and benefits.

Please contact Arthur J. Roberts, MD, Director, Jersey Shore Heart Institute, PO Box 1143, Neptune, NJ 07753. 514C/E

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eferences:
. Slama TG, Sklar SJ, Misinski J, Fess SW.
andomized comparison of cefamandole,
efazolin, and cefuroxime prophylaxis in open-
eart surgery. *Antimicrob Agents Chemother.*
986;29(5):744-747.
. Hurlow RA, Strachan CJL, Wise R. A comparative
udy of the efficacy of cefuroxime for preventing wound
epsis after cholecystectomy. In: Wood C, Rue Y, eds.
efuroxime Update: Royal Society of Medicine International
ongress and Symposium Series Number 38. London, England:
oyal Society of Medicine and Academic Press Inc Ltd; 1981:1-8.
. Gentry LO, Zeluff BJ, Cooley DA. Antibiotic prophylaxis in
pen-heart surgery: a comparison of cefamandole, cefuroxime, and
lin. *Ann Thorac Surg.* 1988;46:167-171.

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Zinacef*
(cefuroxime sodium injection)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in Zinacef* product labeling.

INDICATIONS AND USAGE: Zinacef* is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Lower Respiratory Tract Infections,** including pneumonia, caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), *Haemophilus influenzae* (including ampicillin-resistant strains), *Klebsiella* spp, *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pyogenes*, and *Escherichia coli*.
2. **Urinary Tract Infections** caused by *E coli* and *Klebsiella* spp.
3. **Skin and Skin Structure Infections** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pyogenes*, *E coli*, *Klebsiella* spp, and *Enterobacter* spp.
4. **Septicemia** caused by *S aureus* (penicillinase- and non-penicillinase-producing), *S pneumoniae*, *E coli*, *H influenzae* (including ampicillin-resistant strains), and *Klebsiella* spp.
5. **Meningitis** caused by *S pneumoniae*, *H influenzae* (including ampicillin-resistant strains), *Neisseria meningitidis*, and *S aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea:** Uncomplicated and disseminated gonococcal infections due to *Neisseria gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *S aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. Zinacef has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to Zinacef.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, Zinacef may be used concomitantly with an aminoglycoside (see PRECAUTIONS). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The preoperative prophylactic administration of Zinacef may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (eg, vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. Zinacef should usually be given one-half to one hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of Zinacef has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that Zinacef therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: Zinacef* is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF* IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although Zinacef* rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Zinacef should be reduced in patients with transient or persistent renal insufficiency (see DOSAGE AND ADMINISTRATION), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Zinacef may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest* tablets), but not with enzyme-based tests for glycosuria (eg, Tes-Tape*). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Zinacef.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in mice and rabbits at doses up to 60 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since Zinacef is excreted in human milk, caution should be exercised when Zinacef is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: Zinacef* is generally well tolerated. The most common adverse effects have been local reactions following intravenous administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with intravenous administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in less than 1% of the patients treated with Zinacef and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in less than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (less than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence were seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Toxic epidermal necrolysis, fever, vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see DOSAGE AND ADMINISTRATION). If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Prolonged prothrombin time, pancytopenia, agranulocytosis, thrombocytopenia.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zinacef* product labeling.)

Impaired Renal Function: A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 1 in product package insert).

HOW SUPPLIED: Zinacef* in the dry state should be stored between 15° and 30°C (59° and 86°F) and protected from light. Zinacef is a dry, white to off-white powder supplied in vials and infusion packs as follows:

NDC 0173-0352-31	750-mg* Vial (Tray of 25)
NDC 0173-0354-35	1.5-g* Vial (Tray of 25)
NDC 0173-0353-32	750-mg* Infusion Pack (Tray of 10)
NDC 0173-0356-32	1.5-g* Infusion Pack (Tray of 10)
NDC 0173-0400-00	7.5-g* Pharmacy Bulk Package (Tray of 6)

Zinacef frozen as a premixed solution of cefuroxime sodium should not be stored above -20°C. Zinacef is supplied frozen in 50-mL, single-dose, plastic containers as follows:

NDC 0173-0424-00 750-mg* Plastic Container (Carton of 24)
NDC 0173-0425-00 1.5-g* Plastic Container (Carton of 24)

*Equivalent to cefuroxime

October 1989
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DIVISION OF GLAXO INC
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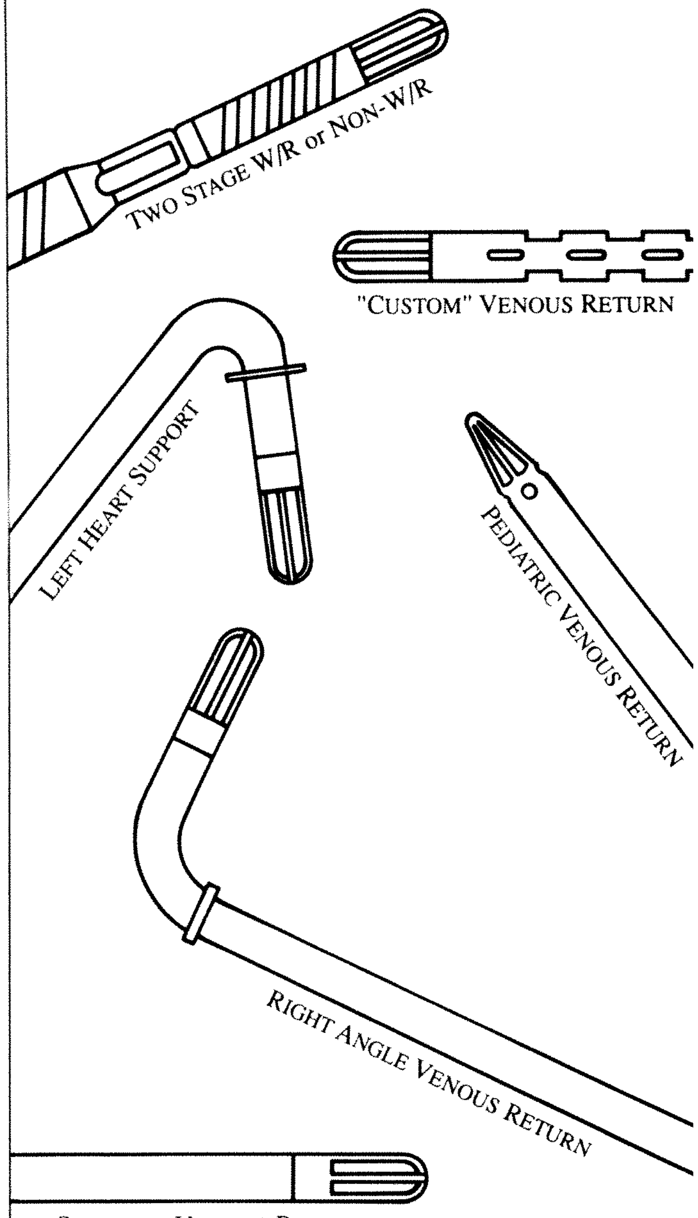

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May 1991

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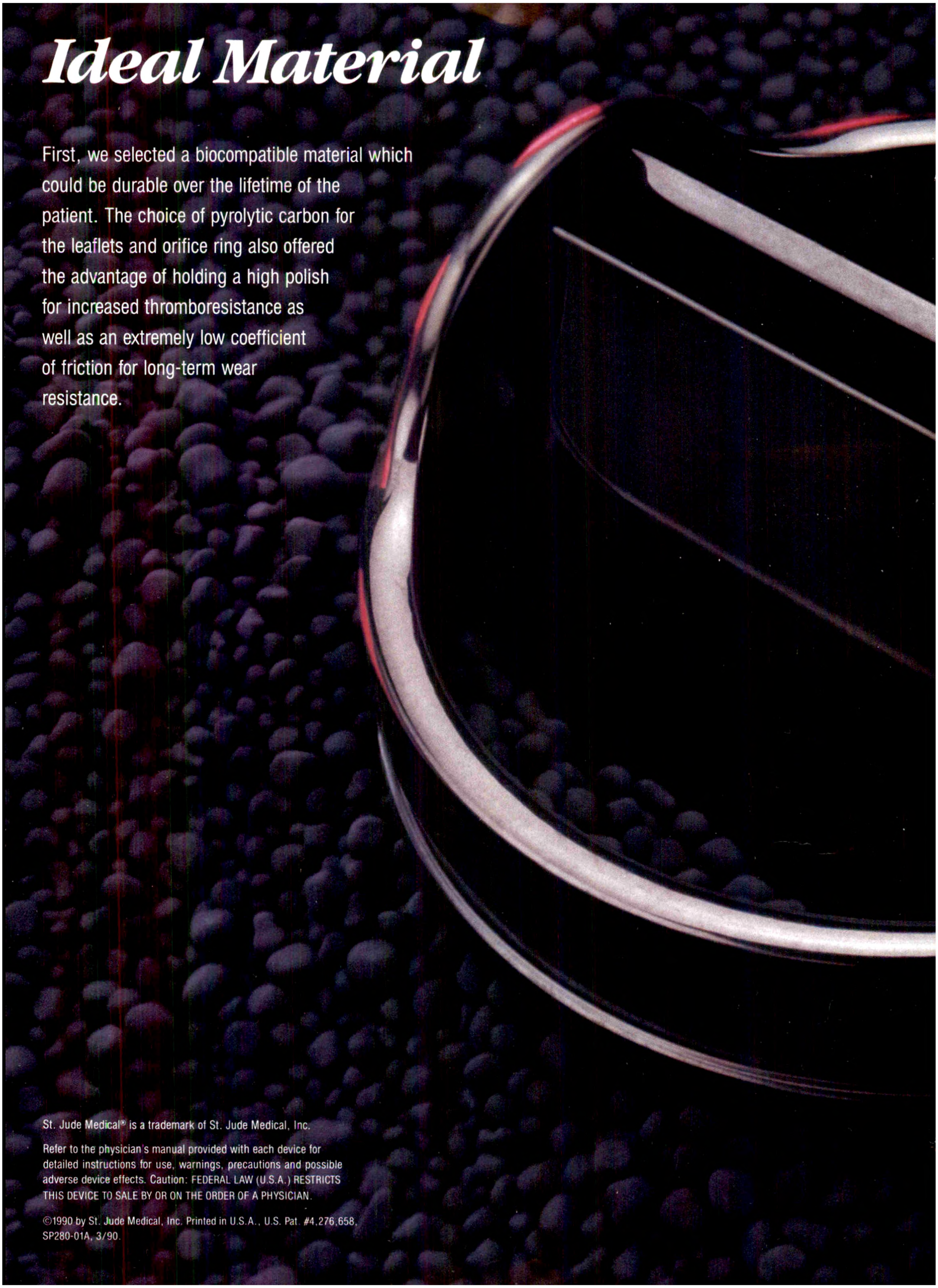

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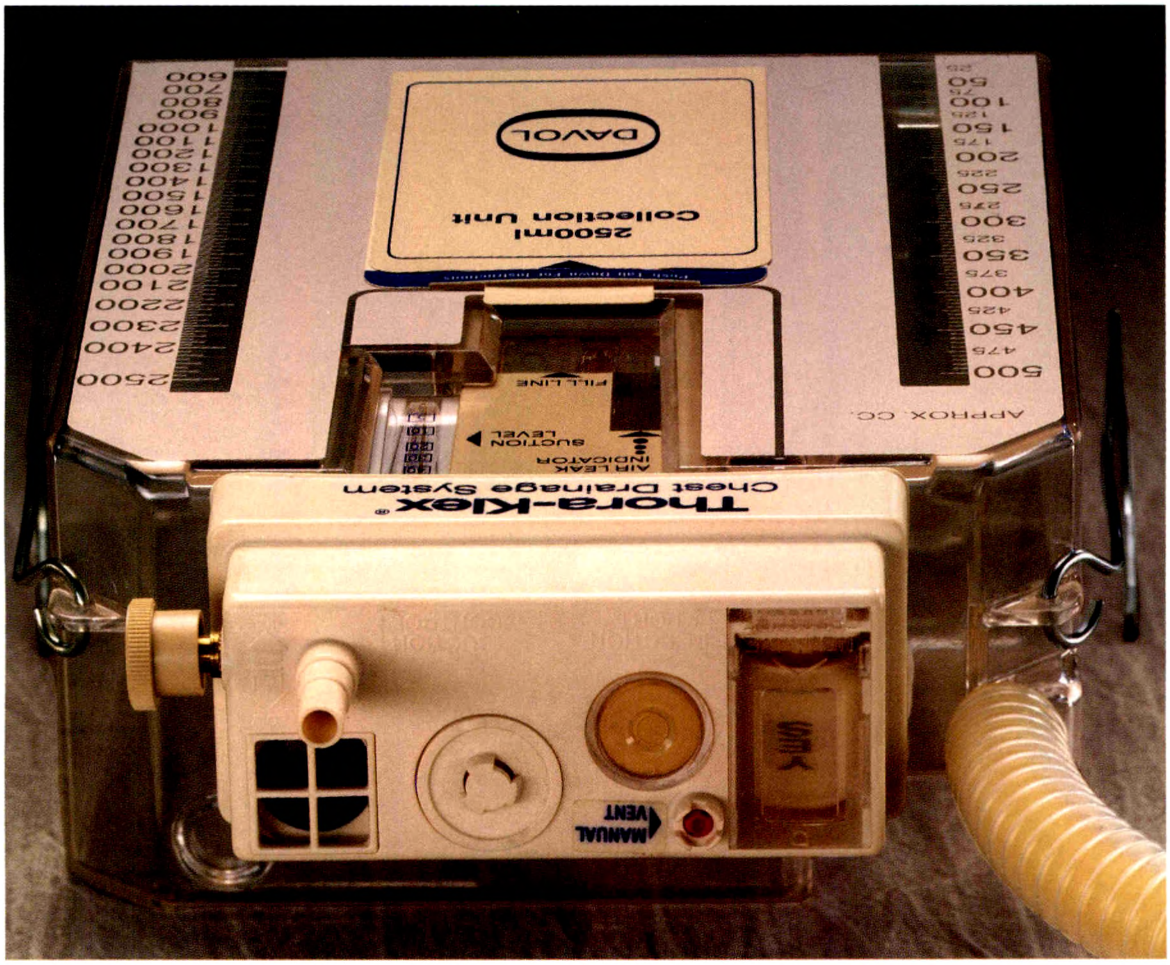

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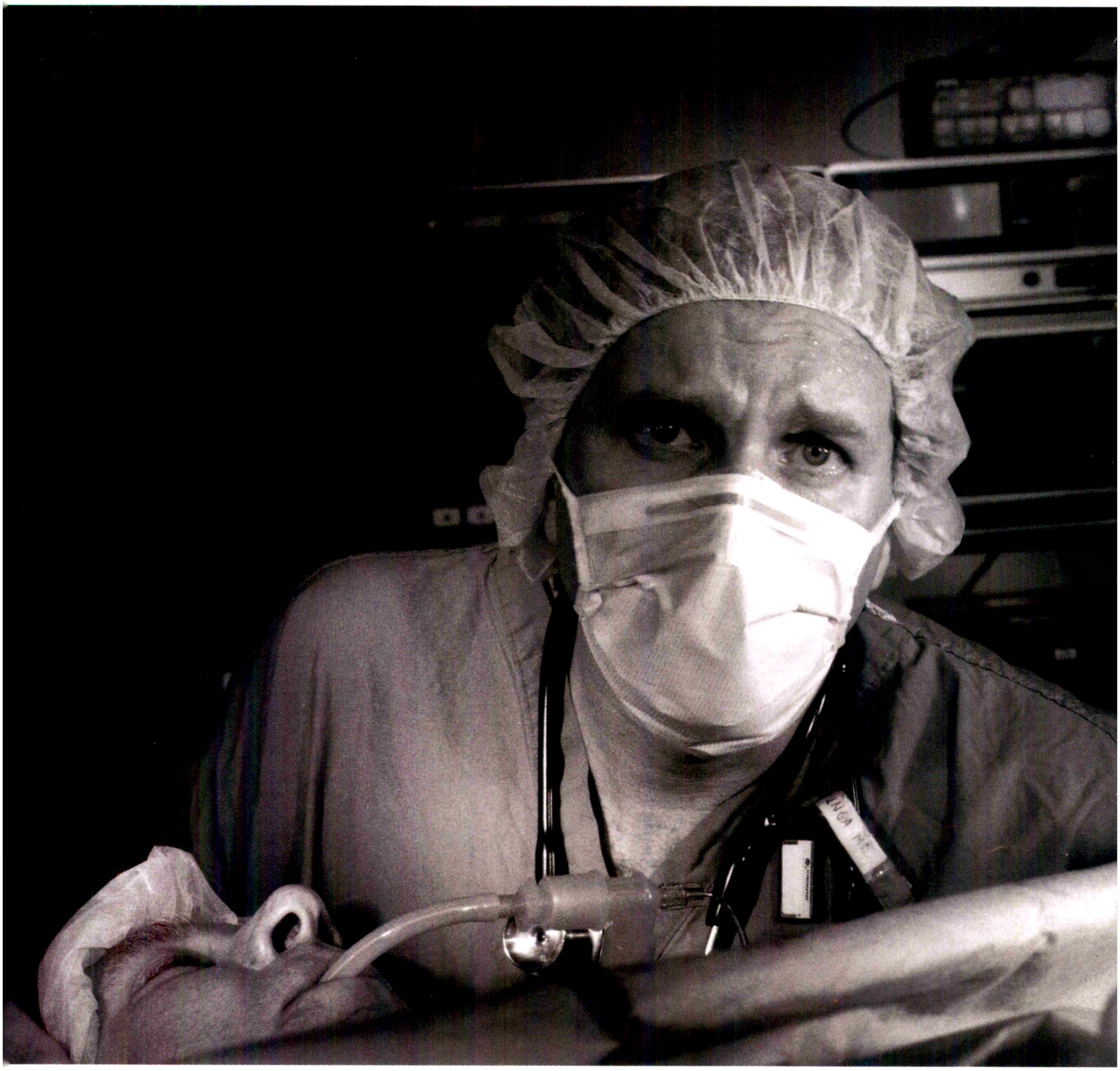

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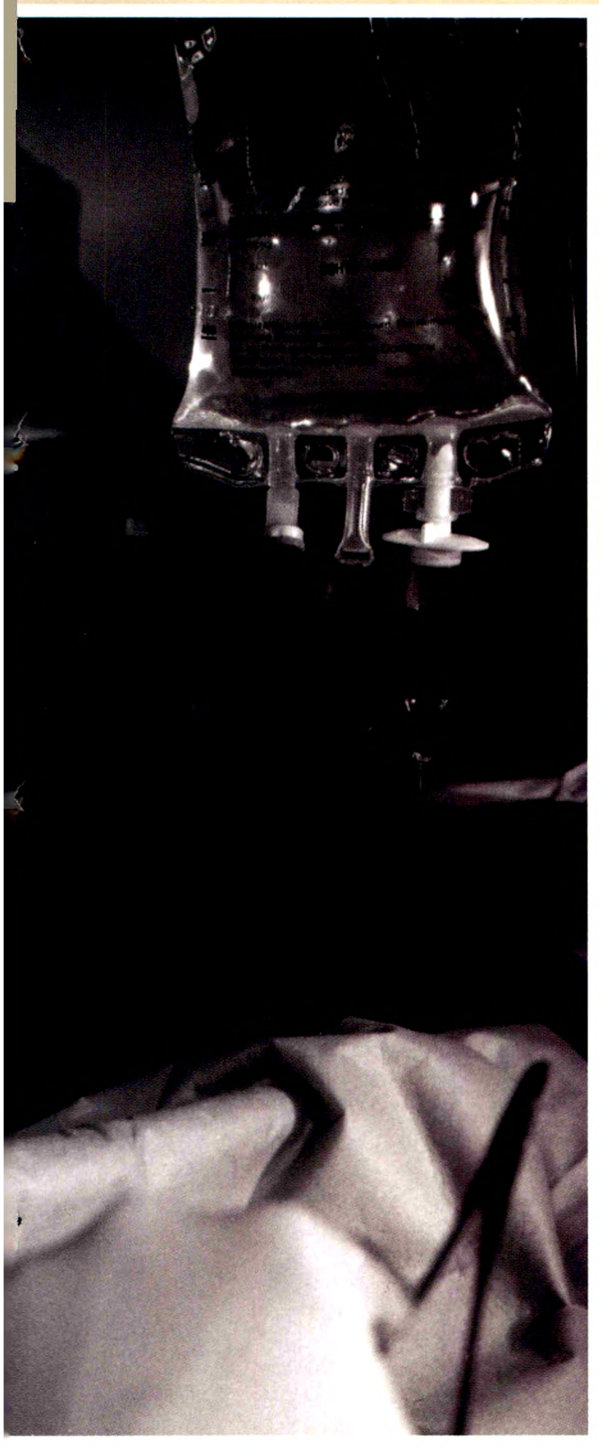

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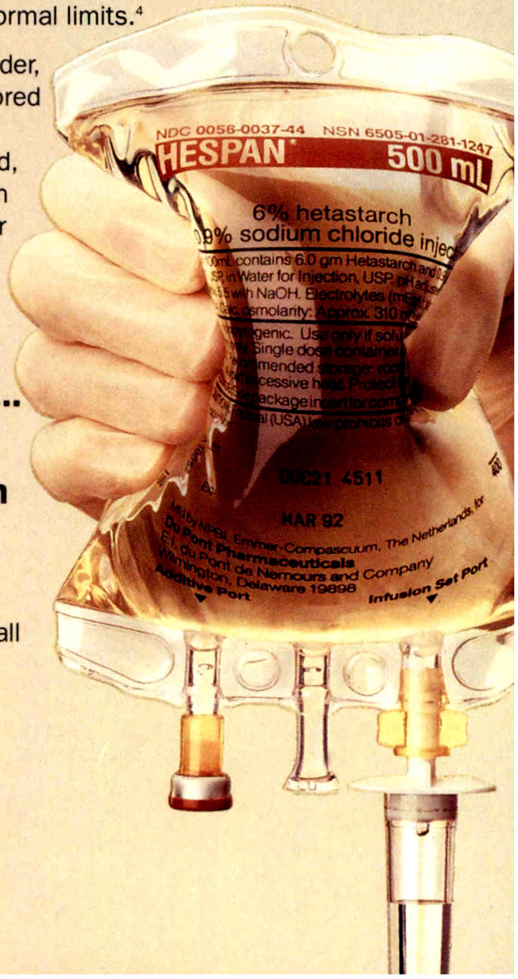

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References: 1. Moggio RA, Rha CC, Somberg ED, Praeger PI, Pooley RW, Reed GE. Hemodynamic comparison of albumin and hydroxyethyl starch in postoperative cardiac surgery patients. *Crit Care Med.* 1983;11:943-945. **2.** Kirklin JK, Lell WA, Kouchoukos NT. Hydroxyethyl starch versus albumin for colloid infusion following cardiopulmonary bypass in patients undergoing myocardial revascularization. *Ann Thorac Surg.* 1984;37:40-46. **3.** Diehl JT, Lester JL, Cosgrove DM. Clinical comparison of hetastarch and albumin in postoperative cardiac patients. *Ann Thorac Surg.* 1982;34:674-679. **4.** Gold MS, Russo J, Tissot M, Weinhouse G, Riles T. Comparison of hetastarch to albumin for perioperative bleeding in patients undergoing abdominal aortic aneurysm surgery: A prospective, randomized study. *Ann Surg.* 1990;211:482-485.

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CONTRAINDICATIONS

HESPAN is contraindicated in patients with known hypersensitivity to hydroxyethyl starch, or with bleeding disorders, or with congestive heart failure where volume overload is a potential problem. HESPAN should not be used in renal disease with oliguria or anuria not related to hypovolemia.

WARNINGS

Usage in Plasma Volume Expansion: Large volumes may alter the coagulation mechanism. Thus, administration of HESPAN may result in transient prolongation of prothrombin, partial thromboplastin and clotting times. With administration of large doses, the physician should also be alert to the possibility of transient prolongation of bleeding time.

Hematocrit may be decreased and plasma proteins diluted excessively by administration of large volumes of HESPAN. Administration of packed red cells, platelets, and fresh frozen plasma should be considered if excessive dilution occurs.

Use over extended periods: HESPAN has not been adequately evaluated to establish its safety in situations other than leukapheresis that require frequent use of colloidal solutions over extended periods. Certain conditions may affect the safe use of HESPAN on a chronic basis. For example, in patients with subarachnoid hemorrhage where HESPAN is used repeatedly over a period of days for the prevention of cerebral vasospasm, significant clinical bleeding may occur.

Usage in leukapheresis: Slight declines in platelet counts and hemoglobin levels have been observed in donors undergoing repeated leukapheresis procedures using HESPAN due to the volume expanding effects of HESPAN and to the collection of platelets and erythrocytes. Hemoglobin levels usually return to normal within 24 hours. Hemodilution by HESPAN and saline may also result in 24 hour declines of total protein, albumin, calcium and fibrinogen values. None of these decreases are to a degree recognized to be clinically significant risks to healthy donors.

PRECAUTIONS

General: Regular and frequent clinical evaluation and complete blood counts (CBC) are necessary for proper monitoring of HESPAN use during leukapheresis. If the frequency of leukapheresis is to exceed the guidelines for whole blood donation, you may wish to consider the following additional studies: total leukocyte and platelet counts, leukocyte differential count, hemoglobin and hematocrit, prothrombin time (PT), and partial thromboplastin time (PTT) tests.

The possibility of circulatory overload should be kept in mind. Caution should be used when the risk of pulmonary edema and/or congestive heart failure is increased. Special care should be exercised in patients who have impaired renal clearance since this is the principal way in which hetastarch is eliminated.

Indirect bilirubin levels of 8.3 mg/mL (normal 0.0–7.0 mg/mL) have been reported in 2 out of 20 normal subjects who received multiple HESPAN infusions. Total bilirubin was within normal limits at all times; Indirect bilirubin returned to normal by 96 hours following the final infusion. The significance, if any, of these elevations is not known; however, caution should be observed before administering HESPAN to patients with a history of liver disease.

HESPAN has been reported to produce hypersensitivity reactions such as wheezing and urticaria. However, hetastarch has not been observed to stimulate antibody formation. If hypersensitivity effects occur, they are readily controlled by discontinuation of the drug and, if necessary, administration of an antihistaminic agent.

Elevated serum amylase levels may be observed temporarily following administration of HESPAN, although no association with pancreatitis has been demonstrated.

Carcinogenesis, mutagenesis, impairment of fertility: Long-term studies of animals have not been performed to evaluate the carcinogenic potential of hetastarch.

Teratogenic Effects: Pregnancy Category C. Animal reproduction studies have not been conducted with HESPAN. It is also not known whether HESPAN can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. HESPAN should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether hetastarch is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when HESPAN is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of HESPAN in children have not been established.

ADVERSE REACTIONS

The following have been reported: vomiting, fever, chills, pruritus, submaxillary and parotid glandular enlargement, mild influenza-like symptoms, headaches, muscle pains, peripheral edema of the lower extremities, anaphylactoid reactions (periorbital edema, urticaria, wheezing) bleeding due to hemodilution (see Warnings), and circulatory overload and pulmonary edema (see Precautions).

DOSAGE AND ADMINISTRATION

Dosage for Acute Use in Plasma Volume Expansion: HESPAN is administered by intravenous infusion only. Total dosage and rate of infusion depend upon the amount of blood or plasma lost and the resultant hemoconcentration. In adults, the amount usually administered is 500 to 1000 mL. Doses of more than 1500 mL per day for the typical 70 kg patient (approximately 20 mL per kg of body weight) are usually not required, although higher doses have been reported in postoperative and trauma patients where severe blood loss has occurred.

Dosage in Leukapheresis

250 to 700 mL of HESPAN to which citrate anticoagulant has been added is typically administered by aseptic addition to the input line of the centrifugation apparatus at a ratio of 1:8 to 1:13 to venous whole blood. The HESPAN and citrate should be thoroughly mixed to assure effective anticoagulation of blood as it flows through the leukapheresis machine.

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration whenever solution and container permit.

The safety and compatibility of other additives have not been established.

HOW SUPPLIED

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40°C does not adversely affect the product.

HESPAN is supplied sterile and nonpyrogenic in 500 mL intravenous plastic infusion containers (NDC 0056-0037-44) and 500 mL intravenous glass bottles (NDC 0056-0037-05).

CAUTION

Federal (USA) law prohibits dispensing without prescription.

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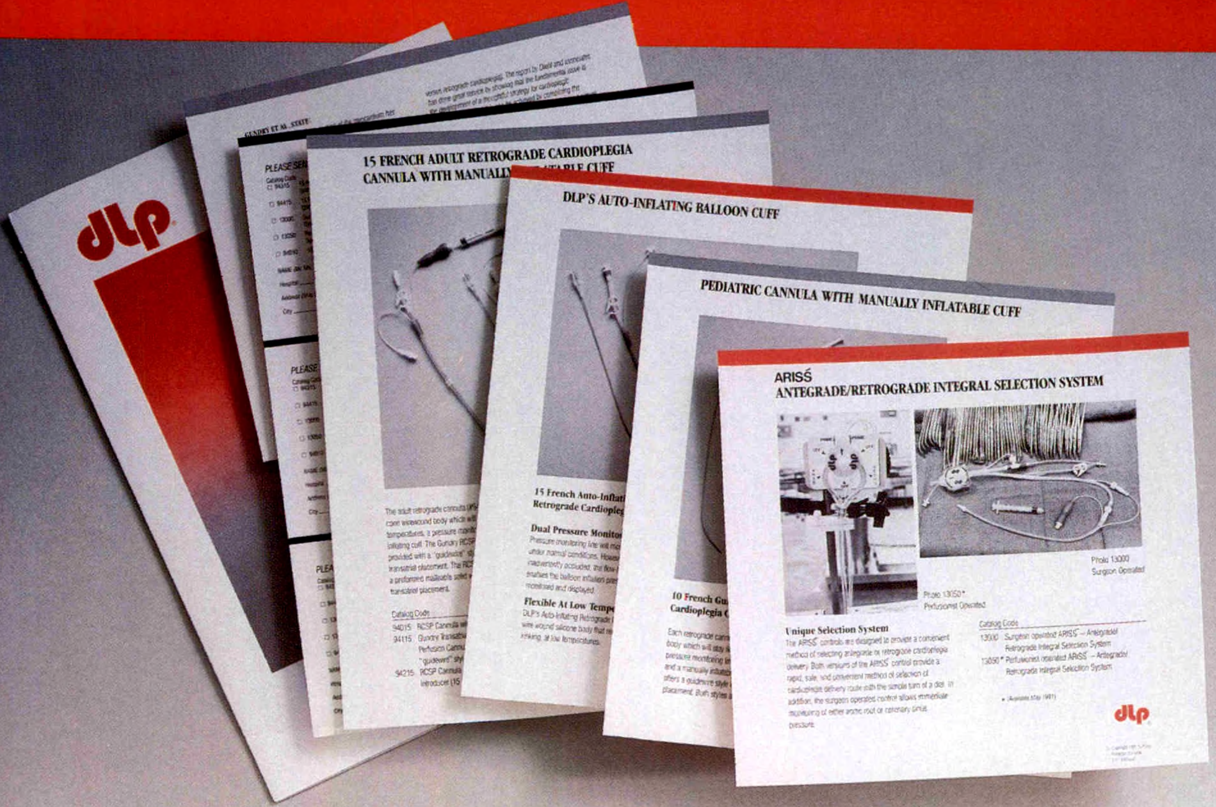
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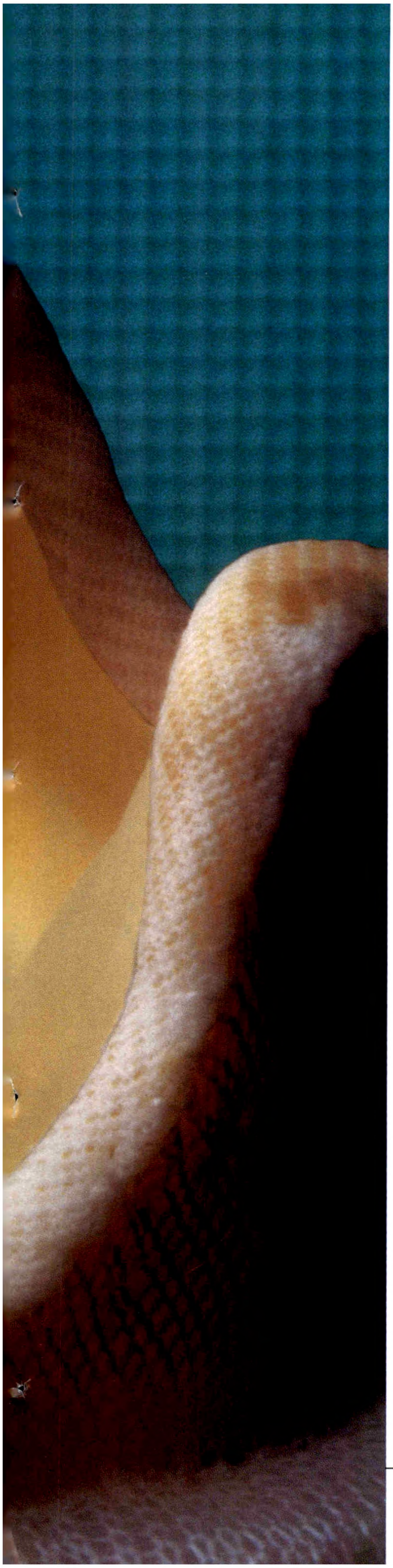

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The Carpentier-Edwards bioprosthesis is intended for use in patients whose aortic or mitral valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic or mitral valve prosthesis which is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. **Warnings:** For Single Patient Use Only In the presence of conditions affecting calcium metabolism or when calcium-containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients under 20 years of age, in patients on a high calcium diet, in the presence of severe systemic hypertension, and in patients who are on maintenance hemodialysis. The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed.Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile**. The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions: 1.** When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Carpentier-Edwards bioprostheses to calcification as compared to other commercially available porcine valves. **Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician. Baxter International Inc. is the owner of the following US patent which covers the products described herein: 4,106,129. Patent numbers in foreign countries supplied upon request. See package insert accompanying product for a full discussion of warnings, contraindications, complications and prescribing information. Carpentier-Edwards® is a registered trademark of Baxter International Inc.

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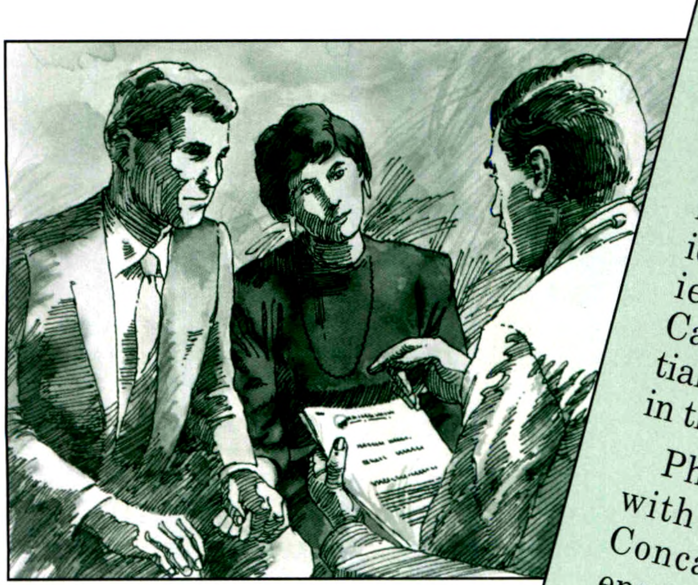

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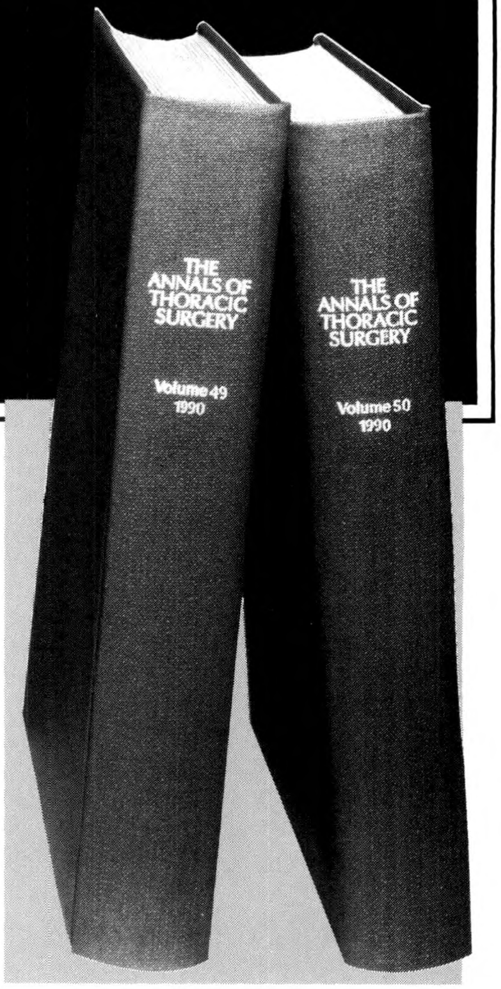
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Penetrating Cardiac Injuries—A Look to the Future

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Before the 17th century it was believed that all cardiac wounds were fatal. In 1642 Tourby was the first to document a spontaneous recovery from a penetrating cardiac injury [1]. This was further documented in 1855 when Purple [2] described 42 cardiac wounds. He found that the right ventricle was most commonly injured and that all wounds were not immediately fatal. In 1871 Colander successfully removed a needle from a heart. The first long-term survivor from a cardiac wound was reported in 1897 by Ludwig Rehn [3]: a young man who had been stabbed in the heart had his wound successfully repaired surgically. Indeed, many of the techniques used even today for repair of cardiac wounds were described in 1926 by Claude Beck [4]. Recently, Moreno and associates [5] described the critical importance of pericardial tamponade in determining survival for penetrating cardiac wounds. The recent development of numerical indices to indicate the severity of penetrating cardiac trauma and attempt to correlate this with survival and prognosis has recently been reported by Ivatury and associates from New York [6].

Over the past 4 years at the University of California, Davis, we have noticed an alarming increase of 24% in the total number of penetrating thoracic injuries. Of even more concern, the number of gunshot wounds to the chest has increased by 39% during the same period. Last year alone 553 patients were admitted to our trauma service with penetrating injuries, of which 121 were penetrating thoracic injuries. In this issue of *The Annals*, Attar and associates [7] have given us some encouragement that appropriate management does favorably alter the outcome.

See also page 711.

In recent years the role of emergency room thoracotomy in penetrating cardiothoracic trauma has been discussed in detail [8]. Regardless of where thoracotomies were done, patients who arrived at the emergency department unconscious and without vital signs suffered excessively high mortality rates, and in some studies this approached 100% [6, 9]. In the study reported in this issue, Attar and associates [7] have reported a 31% survival in patients who arrive at the emergency room with no signs of life! They attribute their impressive success to rapid transport from the field to the emergency department. Nonetheless, 18% of the lowest risk patients who had stable systolic blood pressures of at least 90 mm Hg died of their cardiac wounds. Most patients sustaining penetrating cardiac wounds are in the younger age groups. Hence, if mortality statistics were improved it would represent a major contribution to society. This means that there is opportunity and reason to try to do more to minimize the risk of death among patients who survive penetrating heart wounds long enough to reach hospitals.

As we look to the future there are several relatively new methods of diagnosis and circulatory support that may lead to further progress. For example, two-dimensional echocardiography has been demonstrated to be a very rapid and accurate diagnostic tool for detecting the presence of cardiac injuries [10]. Intraoperative use of transesophageal echocardiography is now becoming a standard procedure in certain open cardiac operations [11]. Our experience using this technique in several patients with cardiac trauma has been favorable. We have been able to detect the presence of intraventricular septal defects, quantitate the degree of left to right shunting, and localize foreign bodies in the heart. Transesophageal echocardiography can be performed expeditiously with the patient asleep on the operating table. In addition to localization of septal defects and foreign bodies in the heart, the technique can also give accurate definition of valvar injuries and demonstrate the degree and severity of valvar regurgitation, and it may also be a useful aide in determining when a patient may need cardiopulmonary bypass for immediate correction of a serious intracardiac defect.

Mattox's group [12] was one of the first groups to use cardiopulmonary bypass in the management of cardiac wounds. Since their report it is now known that with newer techniques of bypass using percutaneous cannulation and extracorporeal support it is possible to begin cardiopulmonary bypass quickly [13]. Moreover, experimental studies in hemorrhagic shock [14] have suggested the possibility and applicability of deep hypothermia and circulatory arrest in certain circumstances of severe penetrating injuries. In addition, Gundry and associates [15] recently reported the ability to resuscitate hearts for transplantation after a 30-minute period of cardiac arrest following exsanguination. The ability to resuscitate a heart after a 30-minute period of complete cardiac arrest is especially exciting. A large body of information is now available about the effects of ischemia and reperfusion on myocardial contractility and function. It is now obvious that the myocardium subjected to low coronary flow exhibits a reversible decrease in force of contraction in a phenomenon known as hibernation. A different type of contractile dysfunction occurs after brief periods of ischemia and reperfusion. This is often referred to as myocardial "stunning" [16]. In our own experience we have seen a number of cases where the offending penetrating injury

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has been repaired, only to lose the patient because of severe myocardial dysfunction. Gundry and associates' work suggests that the heart, after severe exsanguination, may only be stunned or hibernating, and a potential for successful resuscitation exists. Experimental work in this exciting area may show us better ways to resuscitate the myocardium and restore normal contractile force after severe penetrating injuries.

Although Attar and associates [7] showed that most associated injuries and complications did not adversely affect survival after penetrating cardiac injuries, all patients who suffered severe neurological injuries and most patients in whom coagulopathies developed did not survive. To improve results in these groups, research and investigation will have to focus on the earlier detection of irreversible neurological injuries and on ways to avoid the shock-induced coagulopathies that so often occur.

The number of cardiac injuries, unfortunately, will most likely continue to increase throughout the decade. The trauma group at the University of Maryland has made substantial progress toward reducing the morbidity and mortality in these severe cardiac injuries. Despite their impressive morbidity and mortality statistics, there is still work to be done. I anxiously await the results of continued research in the areas of myocardial depression after ischemic insult, the use of cardiopulmonary bypass and possibly hypothermia, the development of better techniques to assess neurological function, and improved methods to treat irreversible shock-induced coagulopathies. It will also be exciting to see if wider use and applications of transesophageal echocardiography and percutaneous cardiopulmonary bypass can lead to even better results.

References

1. Meade RH. A history of thoracic surgery. Springfield IL: Charles C. Thomas, 1961.
2. Purple SS. Statistical observations on wounds of the heart. NY J Med Collat Sci 1855;14:411.
3. Rehn L, Uerber. Petrierend Herzwunden und Herznaht. Arch Klin Chir 1897;55:315.
4. Beck CS. Wounds of the heart. The technique of suture. Arch Surg 1926;1:205.
5. Moreno C, Moore EE, Majure JA, Hopeman AR. Pericardial tamponade: a critical determinant for survival following penetrating cardiac wounds. J Trauma 1986;26:821–5.
6. Ivatury RR, Nallathambi MN, Stahl WM, Rohman M. Penetrating cardiac trauma, quantifying the severity of anatomic and physiologic injury. Ann Surg 1987;205:61–6.
7. Attar S, Suter CM, Hankins JR, Sequeira A, McLaughlin JS. Penetrating cardiac injuries. Ann Thorac Surg 1991;51:711–6.
8. Baker CC, Thomas AC, Trunkey DD. The role of emergency room thoracotomy in trauma. J Trauma 1980;20:848–54.
9. Moore EE, Moore JB, Gallaway AC. Post-injury thoracotomy in the emergency department: a critical evaluation. Surgery 1979;86:590–8.
10. Amsel BJ, Van Der Mas M, De Bock L, van Haasen R, Beeckman C. The importance of two-dimensional echocardiography in the location of a bullet embolus to the right ventricle. Ann Thorac Surg 1988;46:102–3.
11. Marwick T, Currie PJ, Stewart WJ, et al. Echo evaluation of immediate and late failed mitral valve repair [Abstract]. J Am Coll Cardiol 1989;13:115A.
12. Mattox KL, Beall AC. Extending the art: portable cardiopulmonary bypass. J Am Coll Emerg Phys 1975;4:528–31.
13. Shawl FA, Domanski MJ, Hernandez TJ, Punja S. Emergency percutaneous cardiopulmonary bypass support in cardiogenic shock from acute myocardial infarction. Am J Cardiol 1989;64:967–70.
14. Tisherman SA, Safar P, Radovsky A, Peitzman A, Sterz F, Kuboyama K. Therapeutic deep hypothermic circulatory arrest in dogs: a resuscitation modality for hemorrhagic shock with "irreparable" injury. J Trauma 1990;30:836–47.
15. Gundry SR, de Begona JA, Kawauchi M, Bailey LL. Successful transplantation of hearts harvested 30 minutes after death from exsanguination. Ann Thorac Surg (in press).
16. Marban E. Myocardial stunning and hibernation: the physiology behind the colloquialisms. Circulation 1991;83:681–8.

A New Era in Blood Conservation

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Various steps in the history of erythropoietin, from its identification as the hormone regulating erythropoiesis [1] to its subsequent purification [2] and development of the recombinant human product [3], all have taken place in the relatively brief span of only 32 years. Furthermore, the extension of these advances from the basic science and physiology of the hormonal regulation of erythropoiesis to direct application in the clinical treatment of anemia in renal insufficiency occurred within the very short interval of only several years [4, 5]. In addition to the anemia of renal insufficiency, erythropoietin therapy has been shown to be effective for the treatment of other medical anemias such as the anemia seen in patients with acquired immunodeficiency syndrome [6], and has received Food and Drug Administration approval for use in this setting. Studies also have demonstrated that the endogenous erythropoietin response to anemia is inadequate not only in acquired immunodeficiency syndrome [7] but in a variety of settings such as rheumatoid arthritis [8] and cancer [9]. A subsequent clinical trial has shown that erythropoietin therapy can ameliorate the anemia of rheumatoid arthritis [10], and clinical trials of erythropoietin therapy in oncologic settings are in progress. Thus, the promise of erythropoietin as a drug whose initial applicability was focused in the field of renal insufficiency has been quickly extended into a potential tool for the treatment of a variety of anemias associated with chronic disease.

See also pages 764, 767, 823, and 825.

The publication of four articles in this issue of *The Annals of Thoracic Surgery* [11–14] describing the use of erythropoietin therapy in cardiothoracic surgery underscores the important potential of erythropoietin as a surgical blood conservation intervention. Major advances have been made in concepts of blood conservation over the last 30 years, including the use of a nonhematic prime solution [15], intraoperative autologous blood salvage and reinfusion from the operative field [16] or the extracorporeal circuit after cardiopulmonary bypass [17], postoperative collection and autotransfusion of chest drainage [18], and the use of nonhematinic volume expanders and the acceptance of normovolemic anemia [19, 20]. Yet, studies of prevailing practice in patients undergoing routine, primary elective coronary artery bypass grafting reveal that 70% of patients require red blood cell transfusion despite standard blood conservation strategies [21]. The large transfusion requirements in coronary artery bypass grafting can be ascribed to patient demographics such as female sex, preoperative anemia, and patient age [20, 22], as well as to surgical technique [23]. Inappropriate red cell transfusion can be identified in perhaps 15% of patients in this population [21]. Thus, it is apparent that new and innovative methods of blood conservation are needed; pharmacologic interventions are now available both to reduce perioperative blood loss [24, 25] and to increase the erythropoietic response to blood loss [26]. The four reports published in this issue of *The Annals* demonstrate the potential ways in which erythropoietin can be used for blood conservation in the open heart surgical setting: as a preoperative intervention to correct anemia [11] and facilitate autologous blood donation [12], and to increase the erythropoietic response to blood loss postoperatively, in which the endogenous erythropoietin response has been shown to be deficient [13]. In addition, erythropoietin therapy shows great promise as another tool to achieve the ability to perform major surgical procedures without the use of blood transfusions in Jehovah's Witnesses [11, 14]; use of erythropoietin in this clinical setting can serve as a model for its application in all patients in our attempts to reach this elusive goal.

Some issues remain in need of definition for the use of erythropoietin therapy in the surgical setting. Prudent use of this agent suggests that erythropoietin therapy should be linked to ongoing blood losses (either autologous blood donation or perisurgical bleeding) to avoid potential complications related to polycythemia and hyperviscosity in patients at risk [27]. The use of this agent to correct preoperative anemia should ideally be coupled with autologous blood procurement when the hematocrit exceeds 0.33 [28], not only for these safety concerns but also to enhance the effectiveness of this therapy in reducing perisurgical homologous blood transfusions; most blood transfusion support in coronary artery bypass grafting is given on the day of operation and could be best avoided if autologous blood were available preoperatively [21]. The ultimate goal of erythropoietin therapy should be to reduce the need for homologous blood transfusion; erythropoietin should be used only in clinical settings in which this has been shown to occur. Clinical trials that use homologous blood exposure as outcome are currently in progress in a variety of settings to demonstrate this. Finally, questions of optimal dose, route, and interval of administration for erythropoietin therapy have yet to be answered and are the object of study in on-going clinical trials. We eagerly await the results of these studies to fulfill the promise of erythropoietin as a new tool for

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blood conservation and a new alternative to homologous blood transfusion in operations [29].

References

1. Erslev A. Humoral regulation of red cell production. Blood 1953;8:349–57.
2. Miyake T, Kung CK, Goldwasser E. Purification of human erythropoietin. J Biol Chem 1977;252:5558–64.
3. Lin FK, Suggs S, Lin CH, et al. Cloning and expression of the human erythropoietin gene. Proc Natl Acad Sci USA 1985; 82:7580–4.
4. Eschbach JW, Egrie JC, Downing MR, Brown JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. N Engl J Med 1987;316: 3–7.
5. Eschbach JB, Kelley MR, Haley NR, Abels RI, Adamson JW. Treatment of the anemia of progressive renal failure with recombinant human erythropoietin. N Engl J Med 1989;32: 158–63.
6. Fischl M, Galpin JE, Levine JD, et al. Recombinant human erythropoietin for patients with AIDS treated with zidovudine. N Engl J Med 1990;322:1488–93.
7. Spivak SL, Barnes DC, Fuchs E, Quinn TC. Serum immunoreactive erythropoietin in HIV-infected patients. JAMA 1989; 261:3104–7.
8. Baer AN, Dessypris EN, Goldwasser E, Krantz SB. Blunted erythropoietin response to anemia in rheumatoid arthritis. Br J Haematol 1987;66:559–64.
9. Miller CB, Jones RJ, Piantadosi S, Abelloff MD, Spivak JL. Decreased erythropoietin response in patients with the anemia of cancer. N Engl J Med 1990;322:1689–92.
10. Pincus T, Olsen NJ, Russell J, et al. Multicenter study of recombinant human erythropoietin in correction of anemia in rheumatoid arthritis. Am J Med 1990;89:161–8.
11. Fullerton DA, Campbell DN, Whitman GJR. Use of human recombinant erythropoietin to correct severe preoperative anemia. Ann Thorac Surg 1991;51:825–6.
12. Watanabe Y, Fuse K, Konishi T, et al. Autologous blood transfusion with recombinant human erythropoietin in heart operations. Ann Thorac Surg 1991;51:767–72.
13. Levine EA, Rosen AL, Sehgal LR, Gould SA, Egrie JC, Moss GS. Erythropoietin deficiency after coronary artery bypass procedures. Ann Thorac Surg 1991;51:764–6.
14. Gaudiani VA, Mason HDW. Preoperative erythropoietin in Jehovah's Witnesses who require cardiac procedures. Ann Thorac Surg 1991;51:823–4.
15. Cooley DA, Beall AC Jr, Grondin P. Open heart operations with disposable oxygenators, 5 per cent dextrose prime, and normothermia. Ann Surg 1962;72:713.
16. Winton TL, Charrette ESD, Salerno TA. The Cell Saver during cardiac surgery. Does it save? Ann Thorac Surg 1982;33:379–81
17. Moran JM, Babka R, Silberman S, et al. Immediate centrifugation of oxygenator contents after cardio-pulmonary bypass: role in maximum blood conservation. J Thorac Cardovasc Surg 1978;76:510–7.
18. Schaff HV, Haver JM, Beil WR, et al. Autotransfusion of shed mediastinal blood after cardiac surgery: a prospective study. J Thorac Cardiovasc Surg 1978;75:632–41.
19. Geha AS. Coronary and cardiovascular dynamics and oxygen availability during acute normovolemic anemia. Surgery 1976;80:47–53.
20. Cosgrove DM, Loop FD, Lytle BW, et al. Determinants of blood utilization during myocardial revascularization. Ann Thorac Surg 1988;40:380–4.
21. Goodnough LT, Johnston MFM, Toy PTCY, et al. The variability of transfusion practice in coronary artery bypass graft surgery. JAMA 1991;265:86–90.
22. Loop FD, Lytle BW, Cosgrove DM, et al. Coronary artery bypass in the elderly. Indications and outcome. Cleve Clin J Med 1988;55:23–4.
23. Cosgrove DM, Lytle BW, Loop FD, et al. Does bilateral internal mammary artery grafting increase surgical risk? J Thorac Cardiovasc Surg 1988;95:850–6.
24. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
25. Salzman EW, Weinstein MJ, Weinstraub RM. Treatment with desmopressin acetate to reduce blood loss after cardiac surgery. N Engl J Med 1986;314:1402–6.
26. Goodnough LT, Rudnick S, Price T, et al. Increased preoperative collection of autologous blood and recombinant human erythropoietin therapy. N Engl J Med 1989;321:1163–8.
27. Raine AEG. Hypertension, blood viscosity, and cardiovascular morbidity in renal failure: implications for erythropoietin therapy. Lancet 1988;1:97–9.
28. Holland P, ed. Standards for blood banks and transfusion services. 12th ed. Arlington, VA: American Association of Blood Banks, 1989:40.
29. Goodnough LT, Shuck JM. Review of risk, options, and informed consent for blood transfusion in elective surgery. Am J Surg 1990;159:602–9.

Effects of Calcium Chloride Administration on the Postischemic Isolated Rat Heart

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Hypercalcemic reperfusion of the postischemic heart has been associated with ventricular dysfunction and with ultrastructural changes in the mitochondria. The isolated working rat heart model was used to correlate ventricular function, mitochondrial damage, and high-energy phosphate content with degree and timing of hypercalcemia during reperfusion. When administered early during reperfusion, calcium chloride caused a dose-dependent deterioration in ventricular function, whereas calcium augmented function when it was administered after a 15-minute period of normocalcemic reperfusion. Hearts treated with calcium early during reperfusion demonstrated more mitochondrial damage and decreased stores of adenosine triphosphate than those in which calcium administration was delayed. The data indicate that a period of normocalcemic reperfusion should precede calcium administration in the postischemic heart. Mitochondrial damage resulting in decreased synthesis of adenosine triphosphate is likely the cause of ventricular dysfunction associated with calcium administration in the postischemic heart.

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During ischemia, the myocardium gradually becomes depleted of high-energy phosphates, which are necessary for maintenance of normal cellular homeostasis, as well as for the contraction process. Metabolic recovery of the postischemic heart occurs early during reperfusion, whereas return of ventricular function appears to require a longer period of reperfusion [1, 2]. During the early reperfusion period, postischemic myocardium is very susceptible to calcium influx and subsequent injury [3, 4]. Hypercalcemic reperfusion of the postischemic heart results in ventricular dysfunction, and it appears that a period of normocalcemic reperfusion is required before the heart can withstand a calcium challenge [5, 6]. The mechanism by which calcium accentuates ventricular dysfunction in the postischemic heart is unclear. An understanding of this phenomenon at the ultrastructural and histochemical levels is important to establish better mechanisms of myocardial protection during ischemia and reperfusion. The present study correlates mitochondrial damage, depletion of high-energy phosphates, and ventricular function in response to hypercalcemia early during reperfusion and after a period of normocalcemic reperfusion.

Material and Methods

Seven groups of 10 male Sprague-Dawley rats (350 to 400 g) were anesthetized with sodium pentobarbital (60 mg/kg intraperitoneally) and anticoagulated with sodium heparin (2.5 mg injected into the liver). The chest was opened, and the heart was removed and placed immediately in a bath of 4°C Krebs-Henseleit buffer. The aorta was mounted on the perfusion apparatus and the heart was perfused in a retrograde fashion until the left atrium was cannulated. After right-sided decompression was assured by incising the pulmonary artery, the heart was placed in the working mode by allowing antegrade perfusion through the left atrium. Preload was standardized at 10 cm H_2O and afterload was set at 70 cm H_2O. The hearts were allowed to stabilize in the working mode for 20 minutes, during which time baseline hemodynamic measurements were made.

At the end of the 20-minute baseline period, cold (4°C) cardioplegia solution, consisting of Krebs-Henseleit buffer modified to contain 25 mEq/L potassium, was infused for 2½ minutes through the aortic root. After cardioplegic arrest, the heart was subjected to continued ischemic arrest by aortic and left atrial occlusion and immersed in nonoxygenated Krebs-Henseleit buffer at 28°C for 30 minutes.

After ischemic arrest, the hearts were rewarmed with oxygenated perfusate at 37°C in the working mode. Hemodynamic measurements were obtained at 5-minute intervals throughout the reperfusion period. At the completion of reperfusion, the hearts were emptied and frozen in liquid nitrogen for histochemical analysis. Two hearts in each of groups 1, 3, 4, 6, and the control group were fixed for electron microscopy.

Experimental Groups

All hearts underwent identical preischemic time periods and cardioplegic arrest. Hearts in groups 1, 2, and 3 were reperfused in the working mode with $CaCl_2$ added to the Krebs-Henseleit buffer to increase the $[Ca^{2+}]$ to 3.5, 4.5, and 5.5 mmol/L, respectively. Groups 4, 5, and 6 under-

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went 15 minutes of reperfusion with Krebs-Henseleit buffer, followed by a 30-minute perfusion period with [Ca^{2+}] increased to 3.5, 4.5, and 5.5 mmol/L. Controls were reperfused for 30 minutes with Krebs-Henseleit buffer alone ([Ca^{2+}] = 2.5 mmol/L).

Hemodynamic Data Analysis

Hemodynamic data were collected using the Beckman R612 8-channel recorder to measure heart rate and rate of aortic pressure change. Aortic flow was measured directly as a timed collection of perfusate ejected from the aortic outflow tubing. Hemodynamic data are expressed as percent recovery of preischemic baseline.

Histochemical Analysis

Hearts were emptied and frozen between stainless steel tongs cooled in liquid nitrogen and then immersed in liquid nitrogen. Heart tissue was extracted and evaluated for adenosine triphosphate (ATP) and creatine phosphate content by the enzymatic methods previously described [7, 8]. Adenosine triphosphate and creatine phosphate content are reported in micromoles per gram of dry tissue. Analysis of hemodynamic data and values for high-energy phosphate content were performed using paired and unpaired Student's *t* test and analysis of variance.

Ultrastructure

After the inflow and aortic outflow tubing were clamped, the hearts were perfused for 2½ minutes through the aortic root with 3% glutaraldehyde in cacodylate buffer. The left ventricular apex was then cut into 1-mm sections and these were further fixed and processed for transmission electron microscopy. Two hearts in groups 1, 3, 4, 6, and the control group were examined with six to ten micrographs representing each heart. Mitochondrial damage was assessed on a 1 to 4 grading scale, as suggested by Sink and associates [9].

All animals in this study received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

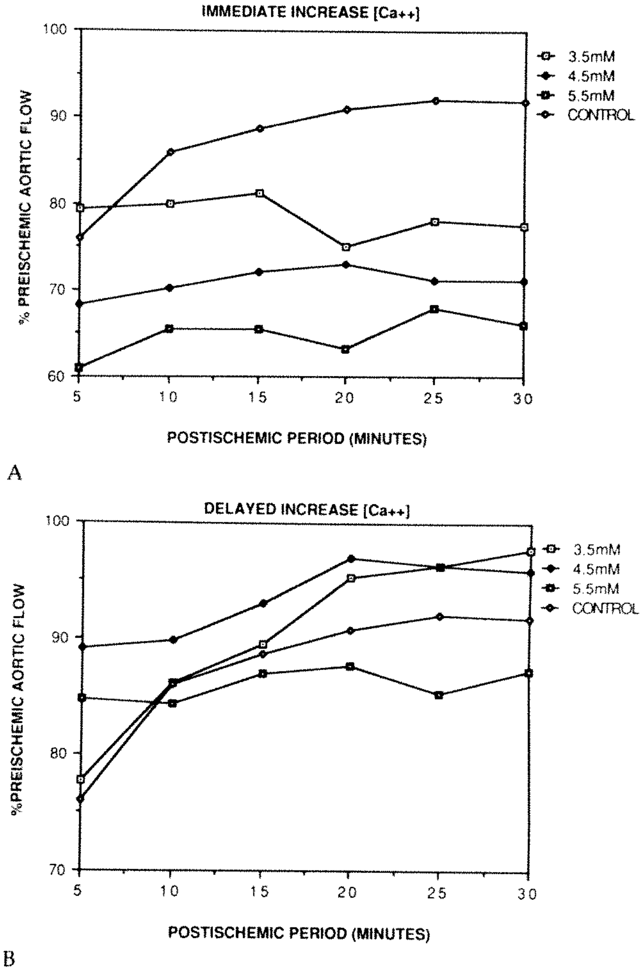

Fig 1. There was a dose-dependent deterioration in return of aortic flow when the reperfusate was made hypercalcemic immediately after ischemia (A). Hearts reperfused with normocalcemic buffer for 15 minutes after ischemia demonstrated augmentation of aortic flow when [Ca^{2+}] of the perfusate was increased to 3.5 mmol/L and 4.5 mmol/L (B). When the [Ca^{2+}] was increased to 5.5 mmol/L, return of aortic flow was diminished.

Results

After the 30 minutes of cardioplegic arrest, control hearts recovered most of their preischemic myocardial function. Heart rate returned to 94.03% of baseline; aortic flow returned to 91.68% of baseline; and there was 96.68% return of rate of aortic pressure change. In those hearts treated with calcium chloride immediately upon reperfusion, there was a dose-dependent deterioration in function. Aortic flow returned to only 76.82% of baseline in group 1, 74.06% in group 2, and 65.68% in group 3 ($p < 0.05$) (Fig 1A). Recovery of heart rate and rate of aortic pressure change in these groups was not significantly different from the control group (Fig 2A).

However, in those hearts in which a 15-minute period of reperfusion was allowed before adding calcium chloride, there was an observed inotropic and chronotropic response. Aortic flow was increased to 96.18% and 96.44% of baseline in groups 4 and 5 (Fig 1B); and heart rate increased to 98.92% and 98.77% of baseline in these groups ($p < 0.05$). There did seem to be an upper limit to the effective dose of calcium in the perfusate. At a calcium concentration of 5.5 mmol/L, a deterioration of function was again seen (Fig 2B).

Histochemically, evidence of high-energy phosphate depletion was observed in hearts subjected to increased calcium concentrations immediately upon reperfusion. Similar to hemodynamic function, the histochemical results were dose-dependent. After 30 minutes of reperfusion with increased calcium concentrations, hearts in groups 1, 2, and 3 had significantly lower stores of ATP and creatine phosphate compared with controls. No high-energy phosphate depletion was seen in any of the hearts treated with calcium chloride if a 15-minute period of reperfusion was allowed before increasing the calcium concentration (Table 1).

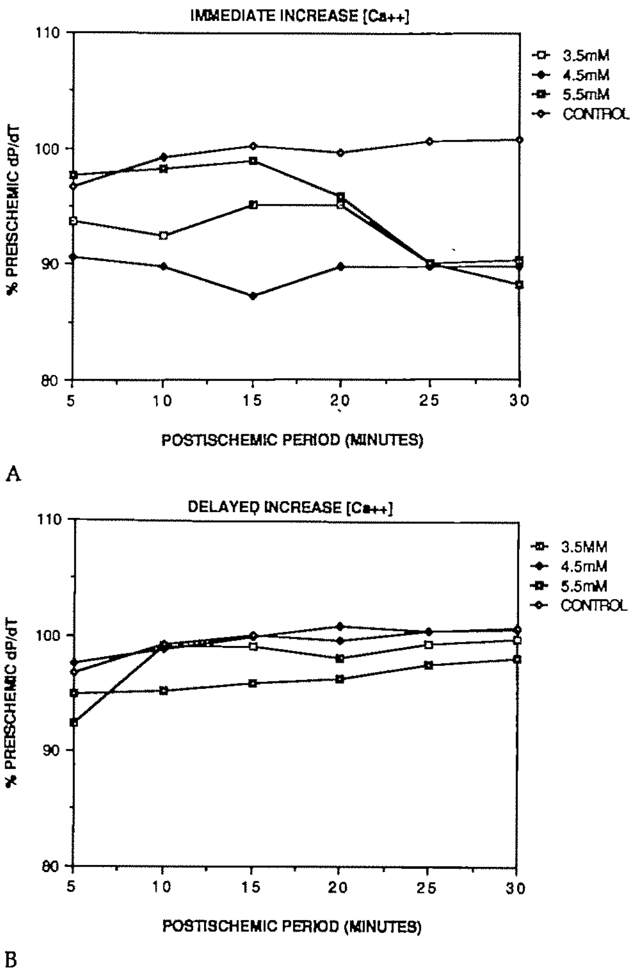

Fig 2. Function deteriorated late in the reperfusion period in groups 1, 2, and 3 as demonstrated by a decrease in rate of aortic pressure change (dP/dT) *after 15 minutes of hypercalcemic reperfusion (A). When 15 minutes of normocalcemic reperfusion preceded hypercalcemic reperfusion in groups 4, 5, and 6, dP/dT returned toward baseline (B).*

Ultrastructurally, hearts treated with calcium immediately upon reperfusion showed more mitochondrial damage than the control hearts. Mitochondrial swelling, membrane disruption, and disruption of the cristae were noted. Hearts treated with calcium later in the perfusion period exhibited fewer of these changes. Dense deposits were seen within the mitochondria of hearts treated with calcium immediately upon reperfusion as well as those treated later during reperfusion (Fig 3). Calcium deposition appeared to be a dose-related occurrence, rather than an occurrence related to the timing of calcium chloride administration. Table 2 summarizes the electron microscopic findings.

Comment

Postischemic functional recovery of the myocardium is dependent on myocardial preservation at the cellular and ultrastructural levels. Hypothermia and cardioplegic arrest have proven benefit in minimizing myocardial cell damage during the ischemic period. By decreasing the time between the onset of ischemia and the onset of asystole, potassium cardioplegia minimizes high-energy phosphate depletion by contracting heart muscle. Hypothermia further reduces high-energy phosphate utilization during ischemia and provides for more available substrate when myocardial work begins during reperfusion [10–12]. High-energy phosphates are depleted during ischemia, however, and mechanical function decreases even when the loss of ATP has been small [1, 13, 14].

Cellular homeostatic mechanisms, such as the ATP-dependent Na^+-K^+ pump and the energy-dependent Ca^{2+} pump of the sarcoplasmic reticulum, must also be preserved during ischemia. As suggested by Kubler and Kate [2], these self-sustaining mechanisms of the myocyte may utilize more of the available ATP during ischemia than the energy-consuming reactions associated with the contractile process. Calcium homeostasis is one of the more labile mechanisms during ischemia. In myocardium made transiently ischemic, intracellular calcium concentration increases, and much of the intracellular calcium can be localized to the mitochondria. In irreversibly injured cells, intracellular calcium can be seen by electron microscopy as dense bodies within the mitochondria in the form of a calcium phosphate precipitate [15]. It appears that sequestration of calcium by the sarcoplasmic reticulum is diminished during the ischemic state and the phenomenon, to a degree, is reversible with reperfusion [16]. Calcium transport into the myocyte is affected by

Table 1. Hemodynamic and Histochemical Data

Group	AF[a]	dP/dT[a]	HR[a]	ATP[b]	CP[b]
Control	91.68 ± 2.42	96.68 ± 3.48	94.03 ± 1.08	68.90 ± 5.74	31.94 ± 2.66
1	76.82 ± 5.87[c]	90.69 ± 2.20	97.76 ± 3.06	55.97 ± 6.17	19.05 ± 2.12[c]
2	74.06 ± 5.28[c]	91.25 ± 2.89	92.02 ± 3.66	52.68 ± 6.52[c]	17.81 ± 1.83[c]
3	65.68 ± 6.37[c]	91.43 ± 3.19	91.56 ± 4.75	40.89 ± 6.43[c]	22.85 ± 1.79[c]
4	96.18 ± 1.41	99.13 ± 0.58	98.92 ± 1.99[c]	78.60 ± 8.25	29.24 ± 2.93
5	96.44 ± 1.24[c]	100.76 ± 0.63	98.77 ± 2.23[c]	62.51 ± 11.4	34.05 ± 5.81
6	86.93 ± 2.09	97.28 ± 1.03	97.60 ± 3.28	83.30 ± 5.80	27.53 ± 3.04

[a] Hemodynamic data are expressed as percent recovery of preischemic baseline values ± standard error of the mean. [b] ATP and CP content are expressed in micromoles per gram dry weight ± standard error of the mean. [c] Significant difference from control at $p < 0.05$.

AF = aortic flow; ATP = adenosine triphosphate; CP = creatine phosphate; dP/dT = rate of change in aortic pressure; HR = heart rate.

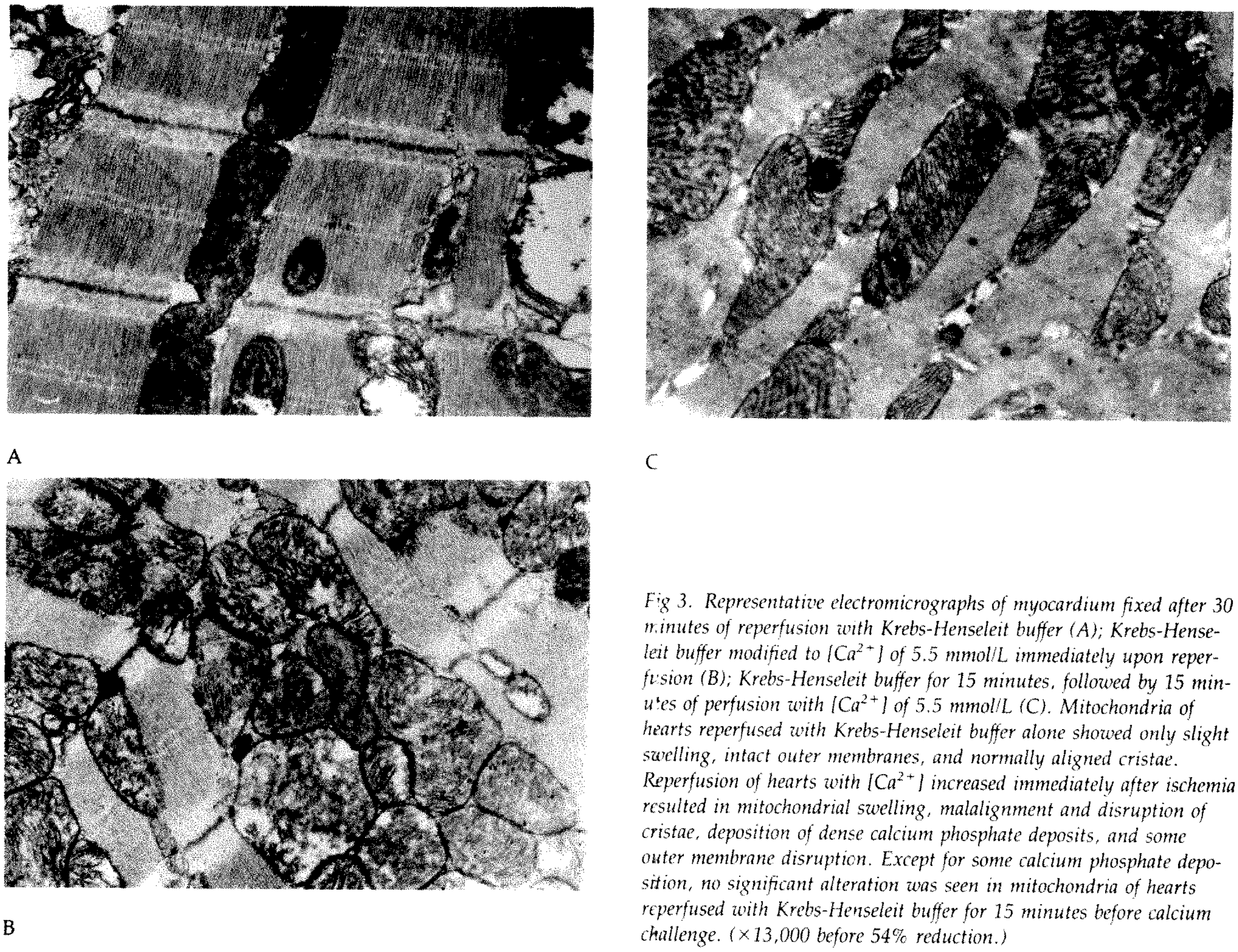

Fig 3. Representative electromicrographs of myocardium fixed after 30 minutes of reperfusion with Krebs-Henseleit buffer (A); Krebs-Henseleit buffer modified to [Ca^{2+}] of 5.5 mmol/L immediately upon reperfusion (B); Krebs-Henseleit buffer for 15 minutes, followed by 15 minutes of perfusion with [Ca^{2+}] of 5.5 mmol/L (C). Mitochondria of hearts reperfused with Krebs-Henseleit buffer alone showed only slight swelling, intact outer membranes, and normally aligned cristae. Reperfusion of hearts with [Ca^{2+}] increased immediately after ischemia resulted in mitochondrial swelling, malalignment and disruption of cristae, deposition of dense calcium phosphate deposits, and some outer membrane disruption. Except for some calcium phosphate deposition, no significant alteration was seen in mitochondria of hearts reperfused with Krebs-Henseleit buffer for 15 minutes before calcium challenge. (×13,000 before 54% reduction.)

extracellular calcium and sodium concentrations [17]. Unfortunately, increasing intracellular calcium, unopposed by effective efflux of sequestered calcium, results in a net increase in ATP utilization and subsequent depletion. In part, ATP depletion can be attributed to an increase in resting tension of the myocyte, but it may also be attributable to the known ability of calcium to uncouple oxidative phosphorylation, prohibiting formation of new ATP [3, 18].

During reperfusion, resynthesis of high-energy phosphates is not immediate, and it requires adequate substrate. The period of time for resynthesis is probably related to the duration of ischemia and the work required during reperfusion. Vary and co-workers [19] reported only 60% recovery of ATP stores in hearts reperfused for 15 minutes after 60 minutes of global ischemia. In hearts arrested for 30 minutes by tissue anoxia, Reibel and Rovetto [1] found that the ATP content was only 50% of the preischemic level after 30 minutes of reperfusion. In their study, postischemic function, in terms of mean ventricular power, had a linear relationship with ATP content. Creatine phosphate repletion occurs early during reperfusion. Previous studies suggest that metabolic recovery in the postischemic heart is completed early during the reperfusion period, provided that cell death has not occurred [16]. In dog hearts arrested with potassium cardioplegia, Chitwood and colleagues [20] showed that metabolic recovery as determined by loss of regional hyperperfusion occurs at a reperfusion time equal to one half the ischemic time.

In the present study, groups 1, 2, and 3 were challenged with high perfusate calcium concentrations immediately upon reperfusion. Groups 4, 5, and 6 were allowed a 15-minute metabolic recovery period (one half the ischemic time) before exposure to higher calcium concentrations. The observation that functional recovery, as measured by aortic flow and rate of aortic pressure change, was adversely affected by early calcium administration was not surprising. Bixler and associates [5] found that reperfusion with normocalcemic or hypocalcemic solutions resulted in better left ventricular functional recovery than reperfusion with hypercalcemic solutions.

The manner in which calcium adversely affects myocardial performance early during reperfusion has been partially elucidated. Lewis and co-workers [4] showed that wall tension increased in postischemic hearts when reperfused with hypercalcemic solutions. Increased wall tension not only increases energy utilization, but also may

Table 2. Morphological Analysis[a]

Group	Edema	Cristal Disruption	Matrical Density	Dense Granules	Membrane Disruption
Control	1+	1+	1+	0	0
Immediate [Ca^{2+}] 3.5 mmol/L	3+	2+	3+	3+	1+
Immediate [Ca^{2+}] 5.5 mmol/L	4+	4+	4+	4+	2+
Delayed [Ca^{2+}] 3.5 mmol/L	1+	1+	1+	1+	0
Delayed [Ca^{2+}] 5.5 mmol/L	2+	2+	1+	2+	1+

[a] Scale from 0 to 4: 0 = normal, 4+ = most abnormal.

decrease diastolic function of the working heart resulting in decreased effective stroke volume.

It is of interest that Yano and co-workers [6] found that allowing a short, initial period of normocalcemic reperfusion abolished the adverse hemodynamic effects of hypercalcemia during early reperfusion. Additionally, we observed that when a period of normocalcemic reperfusion was allowed, hypercalcemic perfusion resulted in an increase in aortic flow. Presumably, during the period of normocalcemic reperfusion, the myocardium repleted its high-energy phosphate store such that the contractile state could be manipulated to perform at levels above the norm.

Intracellular and intramitochondrial calcium accumulation certainly has been implicated in reperfusion injury. Disturbances in calcium homeostasis cause enhancement of free radical production, which in turn results in lipid peroxidation and mitochondrial damage with further loss of ATP [21, 22]. The mitochondria in irreversibly damaged myocardium show vacuolization changes in the mitochondrial matrix with accumulation of dense calcium soaps. Disruption of the mitochondrial membrane is the end result of reperfusion injury with loss of energy-producing activity [22, 23]. In the present study mitochondrial swelling, disruption of cristae, and some mitochondrial membrane disruption were observed in hearts subjected to hypercalcemic reperfusion immediately after ischemic arrest. When the addition of calcium to the reperfusate was delayed, dense deposit accumulation within mitochondria occurred, but very little mitochondrial swelling or disruption of cristae or membranes was observed.

Further, the findings at electron microscopy were correlated with ATP and creatine phosphate content in the heart at the end of the reperfusion, subsequent to any calcium challenge. In hearts subjected to hypercalcemia early during reperfusion, ATP and creatine phosphate content were significantly less than that of control hearts or hearts subjected to hypercalcemia later in the reperfusion period. This finding is consistent with the degree of mitochondrial damage observed and the functional capacity of the hearts reperfused under hypercalcemic conditions. Calcium chloride causes a dose-dependent deterioration of function when administered early during reperfusion. The functional impairment can be attributed, at least in part, to mitochondrial damage and subsequent loss of high energy stores. Conversely, calcium chloride augments myocardial function when administered later during reperfusion of the postischemic heart, albeit at some potential cost.

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References

1. Reibel DK, Rovetto MJ. Myocardial ATP synthesis and mechanical function following oxygen deficiency. Am J Physiol 1978;234:H620–4.
2. Kubler W, Kate AM. Mechanism of early "pump" failure of the ischemic heart: possible role of adenosine triphosphate depletion and inorganic phosphate accumulation. Am J Cardiol 1977;40:467–71.
3. Shine KI, Douglas AM, Ricchiuti NV. Calcium, strontium, and barium movements during ischemia and reperfusion in rabbit ventricle—implications for myocardial protection. Circ Res 1978;43:712–20.
4. Lewis MJ, Grey AC, Henderson AH. Determinants of hypoxic contracture in isolated heart muscle preparations. Cardiovasc Res 1979;13:86–94.
5. Bixler TJ, Gardner TJ, Flaherty JT, Goldman RA, Gott VL. Effects of changes in calcium concentration during postischemic reperfusion on ventricular function and myocardial edema and metabolism. Surg Forum 1977;28:277–8.
6. Yano Y, Riggs TR, Milam DF, Alexander JC. Calcium-attenuated ischemic damage during reperfusion: the time course of the reperfusion injury in the isolated working rat heart model. J Surg Res 1987;42:51–5.
7. Lamprecht W, Stein P. In: Bergmyer HV, ed. Methods of enzymatic analysis. New York: Academic Press, 1963:619.
8. Lowry OH, Passonneau JV. A flexible system of enzymatic analysis. New York: Academic Press, 1972:123.
9. Sink JD, Currie WD, Pellom GL, Hill RC, Chitwood WR, Wechsler AS. Correlation of mitochondrial function and ischemic contracture. J Thorac Cardiovasc Surg 1980;79: 570–8.
10. Hearse DJ, Stewart DA, Braimbridge BC. Cellular protection during myocardial ischemia—the development and characterization of a procedure for the induction of reversible ischemic arrest. Circulation 1976;54:193–202.
11. Kay HR, Rao S, Butchart E, et al. Correlation between ischemic metabolism and postischemic cardiac function. J Surg Res 1978;24:193–200.
12. Wright RN, Levitsky S, Holland C, Feinberg O. Beneficial effects of potassium cardioplegia during intermittent aortic cross-clamping and reperfusion. J Surg Res 1978;24:201–9.

13. Neely JR, Rovetto MJ, Whitmer JT, Morgan HE. Effects of ischemia on function and metabolism of the isolated working rat heart. Am J Physiol 1973;225:651–8.
14. Wood JM, Hanley HG, Entman ML, et al. Biochemical and morphological correlates of acute experimental myocardial ischemia in the dog–IV. Energy mechanisms during very early ischemia. Circ Res 1979;44:52–61.
15. Shen AC, Jennings RB. Myocardial calcium and magnesium in acute ischemic injury. Am J Pathol 1972;67:417–33.
16. Lee KS, Ladinsky H, Stuckey JH. Decreased Ca^{++} uptake by sarcoplasmic reticulum after coronary artery occlusion for 60 and 90 minutes. Circ Res 1967;21:439–44.
17. Wendt IR, Langer GA. The sodium-calcium relationship in mammalian myocardium: effect of sodium deficient perfusion on calcium fluxes. J Mol Cell Cardiol 1977;9:551–64.
18. Lehninger AL. Ca^{++} transport by mitochondria and its possible role in the cardiac contraction-relaxation cycle. Circ Res 1974;34,35(Suppl 3):83–90.
19. Vary TC, Angelakos ET, Schaffer SW. Relationship between adenine nucleotide metabolism and irreversible ischemic tissue damage in isolated perfused rat heart. Circ Res 1979; 45:218–25.
20. Chitwood WR, Hill RC, Wechsler AS. Reperfusion of inflow-limited myocardium following hypothermic potassium-induced cardioplegia. J Thorac Cardiovasc Surg 1984;88: 49–56.
21. Meerson FZ, Kagan VE, Kozler YP, Belkina LM, Arkhipenko YV. The role of lipid peroxidation in pathogenesis of ischemic damage and the antioxidant protection of the heart. Basic Res Cardiol 1982;77:465–85.
22. McCord JM, Roy RS. The pathophysiology of superoxide: roles in inflammation and ischemia. Can J Physiol Pharmacol 1982;60:1346–52.
23. Ganote CE, Angelo J, Safavi S, Katenbech JP. Protection from irreversible hypoxic injury by potassium cardioplegia and hypothermia: effects on contracture, morphology and O_2-enzyme release. J Mol Cell Cardiol 1982;14:587–99.

DISCUSSION

DR PAUL S. BROWN (Chicago, IL): I have been involved in the care of numerous cardiac surgical patients who have required calcium chloride to maintain a cardiac output after removal of the cross-clamp or after sustaining a cardiac arrest, with generally good results. Are the detrimental effects that you have observed with the administration of calcium permanent, or do they resolve at 3 or 4 hours? Also, do you think that the use of calcium chloride in the immediate postbypass or postoperative period trades short-term results for long-term permanent myocardial damage?

DR ABBOTT: We did not carry the experiment more than 45 minutes in reperfused hearts. These data represent only 30 minutes of reperfusion. My general feeling is that if one is going to apply this to the clinical arena, one is probably not looking at application in the patient after arrest, but rather the situation of removing the cross-clamp during cardiopulmonary bypass. We have made it a practice to allow a reperfusion time generally in the area of half the ischemic time before we make the heart work, and that includes calcium administration and other inotropic support.

DR RICHARD E. CLARK (Pittsburgh, PA): When you started your talk, you said you were going to do this to try and find out the mechanism by which calcium may influence cardiac performance in the postischemic interval. If calcium comes into the heart by voltage-sensitive channels as well as non–voltage-sensitive channels, and the presumption is made that it was the voltage-sensitive channels that were at fault in the flood of calcium when you gave calcium immediately, have you been able to figure out other variables that might give you a clue as to why this is happening? That is, the results are observational, but you have not told us what the mechanism is by which these results are achieved. Could you explain that to us in terms of the gates and the nonsensitive channels?

DR ABBOTT: Calcium entry into the reperfused myocyte is dependent on voltage-sensitive and non–voltage-sensitive channels. Tani and Neely [1] demonstrated that reperfusion with hypocalcemic solutions resulted in preserved ventricular function and less extracellular sodium compared with reperfusion with normocalcemic solutions. They concluded that the ATP-dependent Na^+-Ca^{2+} pump was an important pathway for calcium entry during reperfusion. We have been able to demonstrate by electron microscopy less mitochondrial damage with hypercalcemic reperfusion when hearts were arrested with cardioplegic solutions containing a calcium-channel blocker (unpublished data). Some of the injury that is seen is probably due to breakdown of the sarcoplasma reticulum's ability to sequester the calcium, which results in an increase in mitochondrial calcium. I could only speculate on the mechanism of the mitochondrial damage. I think it might have something to do with osmotic fragility of the mitochondria, but I do not believe it has been worked out.

DR ALLAN L. GRAHAM (Forth Worth, TX): Clinically speaking then, if the ionized calcium level is low before you take the cross-clamp off, are you not correcting that until at least 15 minutes or some period after removal of the cross-clamp, and are you paying any attention then to magnesium levels? Are they important?

DR ABBOTT: We have not concentrated on magnesium levels, and it has been our practice to ask the anesthesiologist and the pump technician not to administer calcium until we have achieved a reperfusion time that is equal to half the ischemic time.

Reference

1. Tani M, Neely JR. Mechanisms of reduced reperfusion injury by low Ca^{2+} and/or high K^+. Am J Physiol (Heart Circ Physiol) 1990;258:H1025–31.

Penetrating Cardiac Injuries

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One hundred nine penetrating cardiac injuries were reviewed: 49 gunshot wounds and 60 stab wounds. They were classified into four groups: group 1 (lifeless), 38; group 2 (agonal), 16; group 3 (shock), 33; and group 4 (stable), 22. Thirty-six patients in group 1 (94%) and 8 of 16 patients in group 2 (50%) underwent emergency room thoracotomy; 24 of 33 in group 3 (73%) and 20 of 22 (90%) underwent thoracotomy in the operating room. Twenty-one (38%) of 55 patients undergoing emergency room thoracotomy survived, whereas 47 (87%) of 54 patients undergoing operating room thoracotomy survived. Survival was 12 of 38 (31%) in group 1, 11 of 16 (69%) in group 2, 26 of 33 (79%) in group 3, and 18 of 22 (82%) in group 4 with an overall survival of 67 of 109 (61%). Gunshot wounds of the heart portend a worse prognosis than stab wounds. Survival of gunshot wounds was 20 of 49 (40%) compared with 47 survivors of 60 stab wounds (78%). Aggressive treatment, including emergency room thoracotomy, is justified for lifeless and deteriorating cardiac injury victims.

(Ann Thorac Surg 1991;51:711–6)

Penetrating cardiac injuries continue to increase in proportion to the steady rise in violence in our society. The method of assault has changed from knives and icepicks to more lethal low-velocity hand guns. With the widespread use of rapid medical transportation systems, many of the victims who would have been declared dead at the scene are reaching the trauma centers in urban areas "lifeless" or in extremis. With aggressive resuscitative therapy and emergency room thoracotomy, the salvage rate of these patients can reach up to 35%. This study reviews our experience with penetrating cardiac injuries over the past 23 years.

For editorial comment, see page 701.

Material and Methods

One hundred nine patients with penetrating wounds of the heart were operated on at the University of Maryland Hospital between 1967 and 1990. Most of the patients were brought to the emergency room area within 30 minutes of the time of injury. The directional and anatomical location of the site of injury suggested a presumptive diagnosis of cardiac injury.

Resuscitative measures including endotracheal intubation, volume replacement, and placement of chest tubes were carried out soon after admission to the emergency room. If the patient was "lifeless" or in extremis and did not respond to resuscitative measures, an emergency anterolateral thoracotomy was performed in a designated area of the emergency room. The cardiac tamponade was relieved by pericardiotomy, and bleeding from the cardiac wound was controlled by finger pressure and pledgeted sutures. If the condition of the patient stabilized, then he or she would be moved to the operating room for further repair of the heart wound, if necessary, and control of other thoracic and abdominal injuries. Patients who arrived in stable condition were taken to the operating room for repair of the cardiac injury.

The patients ranged in age from 12 to 84 years (mean age, 32.6 years). There were 97 male and 12 female patients. They were classified into four groups according to their clinical status on admission, as suggested by Ivatury and associates [1] (Table 1). Group 1 comprised 38 patients who arrived unconscious and without vital signs. Group 2 comprised 16 patients who were semiconscious with gasping respiration, a thready pulse, and no measurable blood pressure. Group 3 comprised 33 patients who were hypotensive with a blood pressure of 80 mm Hg or less. Group 4 comprised 22 patients who were in stable condition with a systolic blood pressure of 90 mm Hg or greater. There were 49 (45%) gunshot wounds and 60 (55%) stab wounds; the distribution in each group is shown in Figure 1.

There were 55 emergency room thoracotomies, compared with 54 operating room thoracotomies. Actually, the operating room approach was through a left anterolateral thoracotomy in 31 cases and through a median sternotomy in 23 cases. Pericardiocentesis was performed before thoracotomy in 4 patients early in the series, and pericardial window was performed in 10 patients; two of the latter procedures proved to give false-negative results. The right ventricle was the most commonly involved cardiac chamber in 51 patients, followed by the left ventricle in 30 patients, the right atrium in 11 patients, and the left atrium in 4 patients (Fig 2). Multiple cardiac

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Table 1. Classification According to Clinical Status on Admission

Group	GS Wounds	S Wounds	Total No. of Patients	Clinical Status
1	27	11	38	Unconscious, no vital signs, some sign of life in transit to hospital
2	4	12	16	Semiconscious, thready pulse, gasping respiration, no measurable BP
3	10	23	33	Hypotensive (BP, ≤80 mm Hg), conscious
4	8	14	22	Stable
Total	49 (45%)	60 (55%)	109	

BP = blood pressure; GS = gunshot; S = stab.

chamber involvement was noted in 13 patients: the right and left ventricles in 7, the right ventricle and right atrium in 3, and the right ventricle and left atrium in 1. Involvement of the ventricular septum was noted in 4 patients, transection of the left anterior descending coronary artery proximally in 6 patients, and circumflex coronary artery transection in 2. Mitral valve disruption resulting in mitral regurgitation occurred in a stab wound of the left ventricle. The superior and inferior venae cavae were both disrupted in 2 patients, the inferior vena cava in 4 patients, the superior vena cava in 1 patient, the internal jugular vein in 1 patient, and aorta in 2 patients. A left anterior descending–right coronary artery–ventricular fistula developed in 1 patient.

Most of the cardiac wounds were treated by simple suture repair over Teflon pledgets. Emergency coronary artery bypass grafting was necessitated in 3 patients, with reconstruction of the anterior walls of the right and left ventricles using a Dacron patch in 1 of them.

Associated injuries were present in 77 patients. The lungs were involved in 24 patients, liver in 15, stomach and intestines in 13, colon in 2, diaphragm in 4, spleen in 5, gallbladder in 3, pancreas in 2, kidney in 3, extremity in 6, and spine in 1.

Quantification of the anatomical extent of injury to the heart was done according to the method suggested by Ivatury and associates [1]. The method consists of assigning a risk factor for each thoracic organ based on the reported mortality and morbidity rates from injury to that organ. For example, the heart and major vessels of the thorax receive a score of 5, whereas the lung is given a risk factor of 4. The extent of injury to each organ is graded on a scale of 1 to 5, 1 being minor and 5 being the most severe. The penetrating cardiac trauma index is organ risk factor (5) × injury severity estimate. The product of the risk factor and the estimate of the severity of injury equals the organ injury score. The sum of the thoracic organ injury scores in a patient constitutes the penetrating thoracic trauma index (PTTI). In patients with combined thoracoabdominal injury, the total extent of trauma represented by the penetrating trauma index (PTI) can be expressed by the sum of thoracic and abdominal indices (PTTI + penetrating abdominal trauma index [PATI]). Penetrating abdominal trauma index is measured by the method of Moore and co-workers [2]. The clinical status of the patient is represented by a graded physiologic index (PI) of increasing severity from 5 to 20. Patients who are in stable condition (group 4) have a PI of 5, patients in shock (group 3) have a PI of 10, group 2 patients have a PI of 15, and group 1 patients have a PI of 20.

All data were analyzed using Statistical Analysis System, version 5 programs (SAS Institute, Cary, NC). Nominal data were analyzed using a χ^2 test or Fisher exact probability test for two-by-two tables. Numeric data were analyzed using the Wilcoxon rank-sum test.

Results

The survival rate of penetrating cardiac injuries was related to the time elapsed between injury and initiation of resuscitation, the clinical status on arrival to the emergency room area, the mechanism of injury (whether by

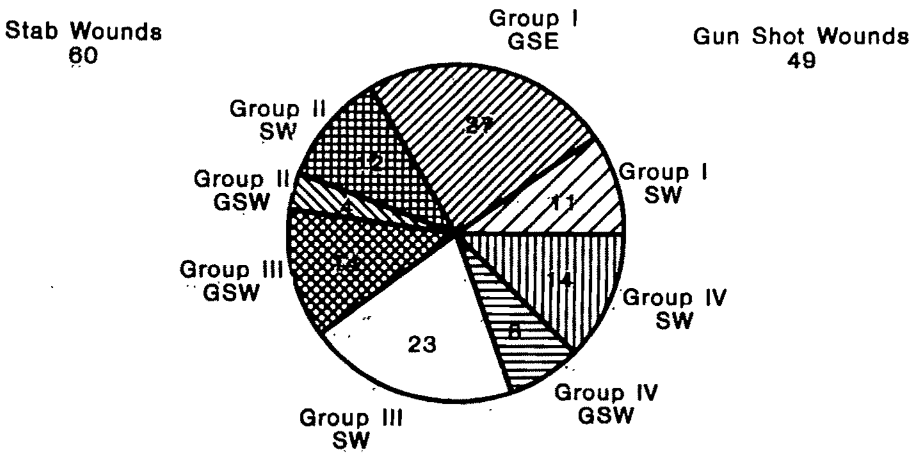

Fig 1. Distribution of patients according to clinical group and mode of penetrating cardiac injury. (GSW = gunshot wound; SW = stab wound.)

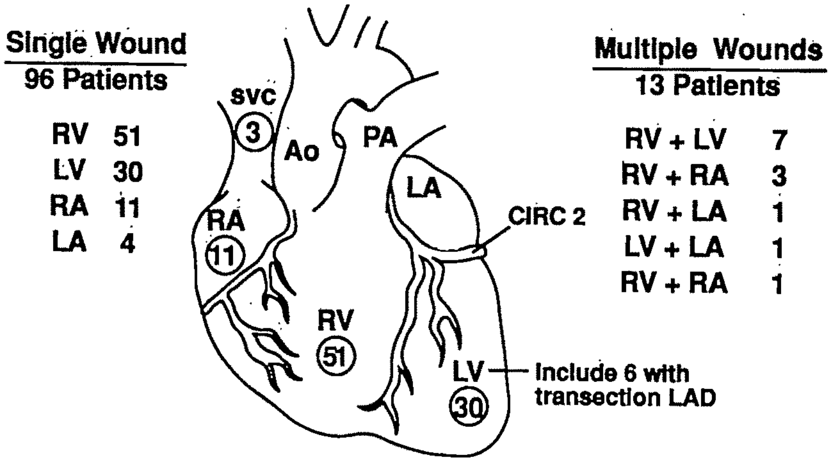

Fig 2. Cardiac chamber involvement in penetrating cardiac injuries. (Ao = *aorta;* CIRC = *circumflex artery;* LA = *left atrium;* LAD = *left anterior descending coronary artery;* LV = *left ventricle;* RA = *right atrium;* RV = *right ventricle;* svc = *superior vena cava.*)

stab wound or gunshot wound), the extent of injury, the need for emergency room thoracotomy for resuscitation, and the presence of cardiac tamponade. The time interval was not a factor in this series of patients, because they were all transported to the emergency room center within 30 minutes of injury. No resuscitative measures were undertaken in the field other than the application of MAST trousers or cardiopulmonary resuscitation when indicated.

There were 12 survivors (31%) among 38 patients who were lifeless on initial presentation (group 1). There were 16 patients in group 2, who were semiconscious but without measurable blood pressure, with 11 survivors (69%). There were 33 patients in group 3, who were in shock, with 26 survivors (79%). Twenty-two patients were stable clinically (group 4) with 18 survivors (82%). As to the mechanism of injury, there were 60 stab wounds and 49 gunshot wounds with 20 surviving the gunshot wounds (a survival rate of 40%) and 47 surviving the stab wounds (a survival rate of 78%): The need for emergency room thoracotomy was very significant, because it reflected the critical clinical condition of the patient. There were 55 patients who required emergency room thoracotomy with 21 survivors (a survival rate of 38%) as compared with 54 patients undergoing operating room thoracotomy with 47 survivors (a survival rate of 87%). When the clinical condition of the patient was correlated with the need for emergency room thoracotomy, there were 36 patients in group 1 with 10 survivors (a survival rate of 27%) and 8 patients in group 2 with 4 survivors (a survival rate of 50%), as compared with the 24 relatively stable patients in group 3 and 20 patients in group 4 who underwent operating room thoracotomy with 19 survivors in group 3 (a survival rate of 79%) and 18 survivors in group 4 (a survival rate of 90%) (Table 2).

The PI representing the clinical status of the patient on admission to the emergency room was very significantly correlated with survival or death ($p < 0.001$). The effect of the thoracic injury superimposed on the cardiac injury was not significant in affecting survival. As to the extrathoracic injuries represented by PATI, they did not affect survival. Quantification of the injuries by the Ivatury method did separate the 49 cardiac injury patients with a mean PATI of 14 from the 60 patients with multiple injuries, who had a mean PATI of 32. The difference was significant ($p < 0.0001$) (Tables 3, 4).

The prognostic score, which represents the sum of the PI and the PTI, was also significantly different for the cardiac injury group alone versus the cardiac injury group with extrathoracic injuries. The mean prognostic score was 27 for the cardiac group, compared with 45 in the group with multiple injuries ($p < 0.0001$). Although the

Table 2. Penetrating Cardiac Injuries: Effect of Clinical Presentations and Treatment on Survival

Group	No. of Patients	Gunshot Wounds			Stab Wounds			Overall Survival
		ERT	ORT	Subtotal	ERT	ORT	Subtotal	
1	38	27 (7)[a]	0	27	9 (3)	2 (2)	11	31%
2	16	2 (0)	2 (2)	4	6 (4)	6 (5)	12	69%
3	33	3 (2)	7 (4)	10	6 (5)	17 (15)	23	79%
4	22	2 (0)	6 (5)	8	0	14 (13)	14	82%
Total	109	34	15	49	21	39	60	
Survival		26%	73%	40%	61%	89%	78%	61%

[a] Numbers in parentheses indicate survivors.

ERT = emergency room thoracotomy; ORT = operating room thoracotomy.

Table 3. Effect of Age and Indices on Survival

Variable	No.	Mean	Standard Error	*p* Value
Age (y)				NS
D	42	30.8	±1.976	
S	67	34.0	±1.941	
PI				0.001
D	42	84.0	±0.664	
S	67	81.0	±0.727	
PTTI				NS
D	42	22.0	±1.776	
S	67	19.0	±1.421	
PATI				NS
D	42	3.66	±1.234	
S	67	3.38	±0.841	
PTI				NS
D	42	26.0	±2.422	
S	67	23.0	±1.648	

D = died; NS = not significant; PATI = penetrating abdominal trauma index; PI = physiologic index; PTI = penetrating trauma index; PTTI = penetrating thoracic trauma index.

Table 5. Complications in Resuscitated Patients

Complication	No. of Patients
Hemorrhagic	
Coagulopathy	9 (3)[a]
Reexploration for bleeding	5 (3)
Sepsis	
Wound infection	7 (7)
Wound dehiscence	5 (5)
Empyema	1 (1)
Cardiopulmonary	
Myocardial infarction	3 (3)
Postcardiogenic shock	2 (1)
Pulmonary embolus	1 (1)
Respiratory insufficiency	1 (1)
Cerebral	
Anoxic encephalopathy	5 (0)
Paraplegia	1 (0)
Total	40 (25)

[a] Numbers in parentheses indicate survivors.

prognostic score was different for the two groups, the survival rate was 63% (31/49) for the cardiac group and 60% (36/60) for the multiple injury group, which was not significant (see Table 3).

The most frequently associated injuries were injuries to the lungs and liver. Complications encountered in resuscitated patients are summarized in Table 5. Forty patients had complications, most of which were nonfatal. The most serious complications were cerebral damage in 5 patients, all of whom died, and coagulopathy in 9 patients, 3 of whom survived.

Comment

Penetrating cardiac injuries have shown a progressive increase over the past two decades. Although the literature indicates the increase is mostly due to gunshot wounds [3, 4] the current series showed a concomitant increase in both gunshot and stab wounds, the implication being that gunshot wounds carry a worse prognosis [4]. They are associated with larger defects in the pericardium and more destruction of myocardial tissue than stab wounds. Subsequently, they are more likely to produce cardiac hemorrhage that results in exsanguination, in contradiction to stab wounds, which produce a small rent in the pericardium that seals off and produces cardiac tamponade. Eighty to 90% of stab wounds demonstrate pericardial tamponade, but only 20% of gunshot wounds of the heart have cardiac tamponade when first seen [4]. Moreno and associates [5] observed that the presence of tamponade improved survival for patients with stab and gunshot wounds of the right as well as the left ventricle. They reported a survival rate of 73% (24/33) in patients with tamponade, compared with 11% (5/44) without its protective effect. Our series does not confirm this observation, because the survival rate was not affected by tamponade.

Table 4. Factors Affecting Survival

Factor	No. of Patients	No. of Survivors	% Survivors	*p* Value
GSW	49	20	40	0.001
SW	60	47	78	
ERT	55	21	38	0.001
ORT	54	46	85	
TAM$^+$	60	40	67	NS
TAM$^-$	49	27	55	
SCH	96	60	62	NS
MCH	13	7	54	

ERT = emergency room thoracotomy; GSW = gunshot wound; MCH = multiple chambers; NS = not significant; ORT = operating room thoracotomy; SCH = single chamber; SW = stab wound; TAM$^+$ = tamponade; TAM$^-$ = no tamponade.

The relative frequency of involvement of the cardiac chambers depends on their anatomical location. The right ventricle is most frequently involved, considering its anterior position, followed by the left ventricle. Karrel and co-workers [4] reported the distribution of involvement of cardiac chambers in a review of 1,802 penetrating cardiac wounds. The right ventricle was involved in 765 cases (42.5%), the left ventricle in 594 cases (33%), the right atrium in 277 cases (15.4%), and the left atrium in 105 cases (5.8%). The intrapericardial great vessels were penetrated in 61 cases (33%). The present series confirms the frequency of this distribution.

The overall survival in this series was 67 of 109 patients (61%), a better survival being accomplished with stab wounds, 47 survivors of 60 (78%), when compared with

20 survivors of 49 gunshot wounds (40%). Moreno and associates [5] reviewed 100 consecutive unselected patients with acute cardiac injuries. Overall salvage was 31%: 27 (47%) of 57 stab wounds and 4 (9%) of 43 gunshot wounds. Tavares and co-workers [6] reported 64 consecutive patients with penetrating cardiac injuries with 45 survivors (70%).

Analysis of the factors affecting survival is summarized in Tables 3 and 4. The most significant factors were the clinical condition of the victim on arrival to the emergency room center represented by the PI, the method of injury (knife or gunshot), and the need for emergency room thoracotomy. The presence of tamponade, the involvement of multiple cardiac chambers, and injury to extrathoracic organs were not statistically significant. This is different from some reported series in the literature. Moreno and associates [5] reported that the presence of tamponade, vital signs, and wound site were the most critical factors for survival. Cardiac tamponade was considered to be a critical independent factor in patient survival, even more influential than presenting vital signs in determining outcome. Ivatury and associates [1] reported 112 patients with penetrating cardiac injuries. Analysis revealed that the indices, penetrating cardiac trauma index and PI, showed an excellent correlation with survival, as did the total extent of trauma (PTI). A composite prognostic score of the sum of PI and PTI demonstrated a significant separation of survivors from nonsurvivors. Our data did not confirm these findings in full. Although penetrating cardiac trauma index and PI correlated well with survival, we could not separate the survivors from nonsurvivors based on the penetrating trauma index.

Serious postoperative complications after repair of cardiac wounds in this series included coagulopathy, sepsis, wound dehiscence, and encephalopathy. Coagulopathy was secondary to cardiogenic and hemorrhagic shock as well as to multiple blood transfusions. Sepsis was frequently due to *Staphylococcus aureus*. Coagulopathy and encephalopathy were generally associated with a fatal outcome. As to the residual and delayed sequelae of penetrating cardiac injuries in this series, ventricular septal defects developed in 4 patients after stab wounds of the heart; 2 underwent repair of the defect, and the other 2 patients had small ventricular septal defects and were asymptomatic. They continue to be treated conservatively. Mitral regurgitation requiring mitral valve replacement developed in 1 patient, and pericarditis requiring pericardiectomy developed in 2 patients. All patients with residual complications who underwent surgical correction survived.

Penetrating cardiac injuries will continue to increase commensurate with increased crime and violence in our cities. Moribund and lifeless patients will be brought to the emergency area. Our experience has demonstrated that aggressive resuscitation, including endotracheal intubation, volume replacement, and chest tube placement followed by resuscitative emergency thoracotomy has resulted in improved survival. Emergency room thoracotomy is indicated in penetrating cardiac injuries in patients who are "lifeless" or in extremis who do not respond to resuscitative measures. Patients with stable vital signs, and hypotensive patients who respond to resuscitative measures, should be transported to the operating room for definitive repair. This selective approach to penetrating cardiac injuries has salvaged a significant percentage of the patients seen "lifeless" or in extremis and has resulted in excellent survival of the patients in stable condition.

References

1. Ivatury RR, Nallathambi MN, Rohman M. Penetrating cardiac trauma: quantifying the severity of anatomic and physiologic injury. Ann Surg 1987;205:61-6.
2. Moore EE, Dunn EL, Moore JB, Thompson JS. Penetrating abdominal trauma index. J Trauma 1981;21:439-44.
3. Ivatury RR, Shah PM, Katsuki I, Ramirez-Schon G, Suarey F, Rohman M. Emergency room thoracotomy for the resuscitation of patients with fatal penetrating injuries of the heart. Ann Thorac Surg 1981;32:377-84.
4. Karrel R, Shaeffer MA, Franaszek JB. Emergency diagnosis, resuscitation, and treatment of acute penetrating cardiac trauma. Ann Emerg Med 1982;11:504-17.
5. Moreno C, Moore EE, Majure JA, et al. Pericardial tamponade: a critical determinant for survival following penetrating cardiac wounds. J Trauma 1986;26:821-5.
6. Tavares S, Hankins JR, Moulton AL, et al. Management of penetrating cardiac injuries: the role of emergency room thoracotomy. Ann Thorac Surg 1983;38:183-7.

DISCUSSION

DR MICHAEL D. HOROWITZ (Miami, FL): Approximately a year ago we had a gentleman brought to the emergency room with an anterior thoracic stab wound. He had had a cardiac arrest and required an emergency room thoracotomy. He was found to have cardiac tamponade due to an injury to the right ventricle. His initial pH was 6.8. After repair and closure, the patient had persistent, profound low cardiac output. An emergency echocardiogram showed a ventricular ejection fraction of approximately 0.15. We considered that we might have missed a coronary artery lesion. Cardiac catheterization showed normal coronary arteries. We placed an intraaortic balloon pump, and within the next 12 to 24 hours his clinical picture changed very impressively. In fact, this man turned around and survived. Late echocardiography showed normal ventricular function.

I attribute much of the cardiac dysfunction to his profound shock and severe acidosis. I would like to ask if you have any experience with use of intraaortic balloon counterpulsation in the group of patients with penetrating cardiac injuries.

DR ATTAR: In our group, we had 2 patients who required intraaortic balloon pulsation after the repair of the cardiac injury. We had only 1 survivor of the 2, which is about 50%. I think it is worthwhile using the intraaortic balloon to support the patients; however, the need for it is really rare, because in most of these patients the injury is localized, especially if it is a stab wound. Stab wounds produce a very small, neat cut in the ventricle in contradistinction to gunshot wounds, which produce substantial tissue injury. We had 1 patient who required reconstruction of the left anterior ventricular wall and the right ventricle as well as a bypass graft to the left anterior descending coronary artery, and he survived. We have been following him up now for 10 years, and he has an ejection fraction of about 0.25.

DR WILLIAM A. COOK (North Andover, MA): Two years ago, the nursing supervisor in a 100-bed hospital where I work asked, "What do you think would be desirable in a thoracotomy kit?" I asked, "What for?" She replied, "The emergency room physicians want to be prepared to do thoracotomies." Here is a group of physicians proposing to do thoracotomies who do not know enough about it to select the instruments.

I would just like to emphasize that there is a great deal of difference between the average community hospital emergency ward and a class I trauma center that probably has an emergency room operating suite with lights, instruments, and all of the other things needed to provide standard thoracotomy in the emergency room setting and probably a full-time thoracic surgical resident. We must not be confused regarding emergency room physicians, now being trained to think about thoracotomy in their training programs, as to what they are capable of doing and equipped to do in an emergency room thoracotomy, especially in the smaller hospital with the occasional patient and no thoracic resident.

In the group of patients we looked at in Dallas, the single most important factor in survival was routine transfer of patients suspected of having a cardiac injury to the operating room, bypassing emergency room stabilization. Even though the patient was simply observed in the operating room, and perhaps never even operated on, if he or she did need to be operated on everything was available. I think this is very important. I would like to be sure that thoracic surgeons are pointing out this aspect of cardiac injury care so the patient does not get lost in the shuffle with emergency room personnel.

DR ATTAR: Dr Cook has raised two issues. The first one is, who should do emergency thoracotomy—the thoracic surgeon, the emergency room surgeon, or the general surgeon? In general, I agree that not every community hospital should have a thoracotomy kit in the emergency room. At the same time, we should not deny the fact that patients with cardiac wounds are brought to the emergency room. The staff of the ambulance service does not know whether the patient has a heart wound or a chest wound that requires operating or if it may be treated conservatively, so they bring the patient to the emergency area. The first person who sees the patient is either the emergency room surgeon or the general surgeon.

In our hospital, it is the general surgical residents who attend to the initial care of the patient. But as soon as the patient hits the emergency room with a presumptive diagnosis of cardiac injury, the thoracic resident, who is on call 24 hours at our university hospital, is called on to supervise the treatment. However, the initial emergency thoracotomy is performed by the general surgical resident in certain conditions. That is, if the patient comes in with cardiac arrest or is under cardiopulmonary resuscitation, or if the patient goes into cardiac arrest, or if there is massive bleeding and deterioration in the emergency room, then the general surgical resident will undertake the emergency thoracotomy. If the patient is in relatively stable condition, having a blood pressure of 80 mm Hg or greater, then he or she can afford to have the luxury of going to the operating room.

There has been a study reported in the literature in which there was a comparison of cardiac wound patients who were operated on in the emergency room versus those who were taken right away to the operating room with a delay of 7 minutes. This 7 *minutes* was very significant as far as survival or death in that series. Therefore, I think we should have an agreed-upon plan between the emergency room staff, the general surgical staff, and the thoracic surgical staff so that when a cardiac emergency is seen in the emergency room, it can be handled properly. In our hospital emergency room, a specific area is designated for emergency thoracotomies and is fully equipped for this procedure.

The second question that Dr Cook raised was whether or not the patients should be taken directly to the operating room. Not every hospital has the luxury of having an operating room ready and available. Sometimes the operating rooms are all full, and you cannot wait until a room opens up. So, you have to take care of the emergency and at least open the chest, control the bleeding, and then take the patient to the operating room when he or she is stabilized for definitive repair.

Cavoatrial Tumor Thrombectomy Using Cardiopulmonary Bypass Without Circulatory Arrest

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Of 29 patients with inferior vena caval tumor thrombus, 14 with supradiaphragmatic extension were deemed suitable for operation. Patients (age, 7.5 to 70 years) had renal cell carcinoma (n = 8), Wilms' tumor (n = 2), transitional cell carcinoma (n = 1), and adrenal carcinoma (n = 3). Seven patients had stage III disease, and 7 patients had stage IV disease. Two patients (group A) had unresectable disease at exploratory celiotomy, 4 patients (group B) underwent tumor thrombectomy without cardiopulmonary bypass, and cardiopulmonary bypass was employed in 8 patients (group C). Three of 8 group C patients had Budd-Chiari syndrome at diagnosis. Cardiopulmonary bypass with moderate hypothermia, and inferior vena caval interruption (clip or filter), was employed in all patients. There were no perioperative deaths. Transient neurological impairment was observed postoperatively in 2 patients. Coagulopathy developed in 1 patient who had hepatic encephalopathy and Budd-Chiari syndrome preoperatively and in another patient in whom protamine could not be administered. No patient had acute renal failure requiring hemodialysis. Median survival is 41 and 17 months in groups B and C, respectively. Some authors have advocated profound hypothermia and circulatory arrest in these patients. We find that satisfactory visualization and excision can be performed with cardiopulmonary bypass and moderate hypothermia, avoiding potential renal, hepatic, neurological, and septic complications associated with circulatory arrest.

(Ann Thorac Surg 1991;51:717–22)

Although 4% to 10% of patients with renal cell cancer have transluminal tumor propagation into the inferior vena cava (IVC), radical excision of these renal, and by inference adrenal, tumors has been the accepted surgical approach since the mid-1970s when Marshall, Skinner, and their associates [1, 2] demonstrated that long-term survival could be achieved in these patients. However, controversy exists regarding the best operative approach to tumors with extension into the suprahepatic IVC and right atrium. Some have suggested that as the level of extension progresses in a cephalad direction prognosis worsens, with only a rare patient surviving 5 years [3]. Others have proposed that operative removal with profound hypothermia and circulatory arrest should be used to allow complete removal of the tumor thrombus, thereby possibly extending survival [4–7]. We have reviewed our results with cavoatrial tumor thrombectomy over the past 10 years since the report by Prager and associates [8], and this report summarizes our experience with surgical treatment of these difficult patients.

Material and Methods

From May 1979 through September 1989 we have seen 29 patients with vena caval tumor extension. In 14 of these patients tumor extended above the diaphragm or into the right atrium. Two patients had unresectable disease at operation (group A), 4 patients had tumor thrombectomy without cardiopulmonary bypass (group B), and cardiopulmonary bypass was used in 8 patients (group C). Four patients (3 group C, 1 group B) had massive ascites and evidence of hepatic venous obstruction (Budd-Chiari syndrome). Eight patients had renal cell carcinoma, 3 had adrenal cortical carcinoma, and 2 had Wilms' tumor. One patient had transitional cell carcinoma originating in the renal pelvis. Nine tumors were right sided and five were left sided. There were 6 male and 8 female patients. Ages ranged from 7.5 years, in a patient with Wilms' tumor, to 70 years (average, 48.5 years; standard deviation, 20.5 years). Follow-up now extends an average of 30 months (standard deviation, 30 months; range, 2 to 99 months). Details of the patient characteristics and pathology are presented in Table 1.

Although details of the operative procedures varied, several factors remained constant. All tumors were exposed through a median sternotomy combined with a midline celiotomy. Nephrectomy or adrenalectomy was performed first, usually after control had been obtained around the intrapericardial IVC with an umbilical tape, taking care not to manipulate the right atrium or vena cava. The falciform, coronary, and triangular ligaments of the liver were divided and the liver was rolled to the patient's left side. The diaphragm was split into the

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Table 1. Patient Data

Patient No.	Age (y)	Sex	Symptoms	Histology	Side	Stage
1	63	M	Budd-Chiari	RCC	R	III
2	7.5	M	ABD Pain	Wilms'	L	IV
3	59	M	Budd-Chiari	RCC	R	III
4	57	F	Budd-Chiari	RCC	L	III
5	57	F	LE swelling	RCC	R	IV
6	26	F	Cushing's	Adrenal	R	III
7	55	F	Cushing's	Adrenal	R	III
8	64	F	LE swelling	TCC	L	IV
9	59	M	LE swelling	RCC	R	IV
10	61	M	LE and ABD swelling	RCC	L	IV
11	8	F	ABD pain	Wilms'	R	III
12	70	M	LE swelling	RCC	R	III
13	55	F	ABD swelling	RCC	L	IV
14	38	F	Budd-Chiari	Adrenal	R	IV

ABD = abdominal; LE = lower extremity; RCC = renal cell carcinoma; TCC = transitional cell carcinoma.

central tendon, toward the IVC. Hepatic venous branches to the caudate lobe were usually divided to allow maximum mobilization of the liver and exposure of the IVC. In this fashion, the infrahepatic, intrahepatic, and suprahepatic portions of the vena cava were exposed completely, and the level of tumor extension was confirmed. Most renal or adrenal tumors with transluminal propagation into the IVC do not extend above the hepatic veins and may be safely removed without cardiopulmonary bypass using this exposure. If cardiopulmonary bypass was employed heparin was administered and cannulation performed with superior vena caval drainage and ascending aortic return. In those patients with a patent IVC below the renal veins, additional venous drainage was accomplished by direct cannulation of the IVC near the iliac bifurcation or alternately through one iliac or femoral vein.

Cardiopulmonary bypass was instituted, and the patients were cooled to 30° to 32°C. Tumor thrombectomy was performed through separate incisions in the infrahepatic IVC and right atrium. The cardiotomy suction was used to aspirate hepatic venous and coronary sinus return, and the tumors were carefully peeled from the vena cava and right atrium. All hepatic venous orifices were inspected. If blood return obstructed visualization, a Pringle maneuver was performed, the ascending aorta was cross-clamped, and cardioplegic solution was administered. We have found this rarely necessary. The cavotomy and right atriotomy were repaired as air was expelled from the right atrium. Vena caval interruption has been performed in all adult patients. In earlier patients, a Miles clip was placed around the infrarenal IVC. In later years, a Greenfield filter has been placed into either the infrarenal or suprarenal IVC through the right atriotomy just before completion of the atrial suture line. Cardiopulmonary bypass was weaned and terminated after the patient was warmed to 37°C.

Data are presented as mean with standard deviation (SD), and statistical significance is noted at the p less than 0.05 level. Survival statistics were calculated using NCSS software (NCSS, Kaysville, UT) and are presented with 70% confidence limits (CL).

Results

A summary of patient groups based on operative approach listing blood loss, transfusions, length of hospital stay, complications, duration of follow-up, and survival is included in Table 2.

Two patients (group A), both with stage IV renal cell carcinoma, were believed to have unresectable disease at the time of exploration. One patient had direct extension of tumor into the liver and diaphragm. The other had extensive retroperitoneal spread and involvement of the bladder. Although neither patient suffered a perioperative complication, both died of extensive metastatic disease within 3 months.

Four patients (group B) had vena caval tumor thrombectomy without cardiopulmonary bypass. Two patients had renal cell carcinoma, 1 had adrenal cortical carcinoma, and 1 had Wilms' tumor. In these cases, tumor extension above the diaphragm was minimal, which allowed early control of the intrapericardial IVC and safe placement of a vascular clamp at the cavoatrial junction during tumor thrombectomy from below. Blood loss in these operations averaged 2,750 mL (SD, 1,760 mL; range, 1,500 to 4,000 mL). Average blood products transfused in this group of patients were 13 units of blood, 2 units of platelets, and 2 units of fresh frozen plasma. Hospital stay in this group of patients averaged 18.5 days (SD, 3.5 days; range, 16 to 21 days). There were no perioperative complications noted in this group of patients. Two patients died due to extensive metastatic disease 15 and 41 months postoperatively. The remaining 2 patients are alive with no evidence of metastatic disease 87 and 99 months postoperatively.

Eight patients (group C) underwent tumor thrombectomy on cardiopulmonary bypass for extensive atrial or supradiaphragmatic vena caval tumor involvement. Four patients had renal cell carcinoma, 2 patients had adrenal cortical carcinoma, and 1 each had transitional cell carcinoma and Wilms' tumor. Average blood loss in these patients was 3,200 mL (SD, 1,262 mL; range, 900 to 4,500 mL). Blood loss has recently declined (approximately 900 mL) with the use of the Cell Saver. All patients received blood transfusions perioperatively. Platelet transfusions were required in 6 patients and fresh frozen plasma in 5 patients. Reconstituted cryoprecipitate was administered to 1 patient. Blood products transfused averaged 10 units (SD, 5.9 units) of blood, 6 units (SD, 7.2 units) of platelets, and 2 units (SD, 3.0 units) of fresh frozen plasma. Average pump time was 72 minutes (SD, 17 minutes; range, 42 to 95 minutes). Hospital stay averaged 20 days (SD, 16

Table 2. Operative and Postoperative Data

Patient No.	Blood Loss (mL)	Transfusions (B/PLT/FFP/CPPT)	Hospital Stay (d)	Complications	Alive	Follow-up (mo)
Group A						
9	250	0	18	None	N	3
10	500	0	21	None	N	3
Group B						
11	1,500	3/0/0/0	21	None	Y	99
12	. . .	. . .	18	None	Y	75
13	. . .	. . .	19	None	N	41
14	4,000	24/5/5/0	16	None	N	15
Group C						
1	4,500	22/18/8/6	18	COAG, ABNL LFT, RA ANEUR, dementia	Y	29
2	2,600	6/1/4/0	20	None	N	9
3	4,000	10/16/2/0	20	ABNL LFT	N	19
4	4,000	11/1/0/0	18	ABNL LFT, dementia	Y	51
5	4,500	12/0/0/0	10	None	N	9
6	900	2/0/0/0	12	None	Y[a]	17
7	3,500	14/0/7/0	18	COAG, REOP, groin wound	Y	29
8	3,000	8/0/6/0	61	Dementia	N	2

[a] With metastases.

ABNL LFT = transient elevation of transaminase and bilirubin levels; B = blood; COAG = coagulopathy; CPPT = cryoprecipitate; FFP = fresh frozen plasma; PLT = platelets; RA ANEUR = radial artery false aneurysm; REOP = reoperation.

days; range, 7 to 61 days). There were no operative deaths.

In 1 patient with extensive transitional cell carcinoma invading the vena cava from the renal pelvis, metastatic and recurrent vena caval disease developed; this patient died 2 months postoperatively. Three patients died of metastatic disease 9, 9, and 19 months after operation. It should be noted that early in this series all shed blood was discarded at the time of tumor thrombectomy to minimize the possibility of tumor cell transmission and subsequent metastases. This policy has been abandoned in recent years. Four patients are alive with no evidence of disease at 17, 29, 29, and 51 months after operation. Serious perioperative morbidity occurred in 3 patients. Transient dementia occurred in 2 patients. In 1 patient with Budd-Chiari syndrome and hepatic encephalopathy preoperatively, a diffuse coagulopathy requiring blood product transfusions developed after reversal of heparin. Another patient required mediastinal reexploration for postoperative bleeding. This patient experienced profound hypotension on two separate occasions after a test dose of protamine sulfate despite histamine$_1$ and histamine$_2$ receptor blockade [9], and the heparin was not reversed. There were 5 minor complications in 3 patients: 1 obese diabetic patient had superficial groin wound separation after femoral venous cannulation, which healed without difficulty. A late radial artery false aneurysm developed in another patient. Three patients with Budd-Chiari syndrome preoperatively had transient elevation of serum transaminase and bilirubin levels postoperatively. No patient experienced pulmonary embolization, sepsis, cerebrovascular accident, myocardial infarction, or renal failure.

Kaplan-Meier product-limit estimate of survival for all patients is presented in Figure 1: Actuarial survival at 1, 3, and 5 years is 64% (CL, 77% and 51%), 49% (CL, 63% and 35%), and 37% (CL, 52% and 22%), respectively. Median survival for the entire group is 18.5 months. Actuarial survival in patients based on operative approach (with and without bypass) is presented in Figure 2. Though

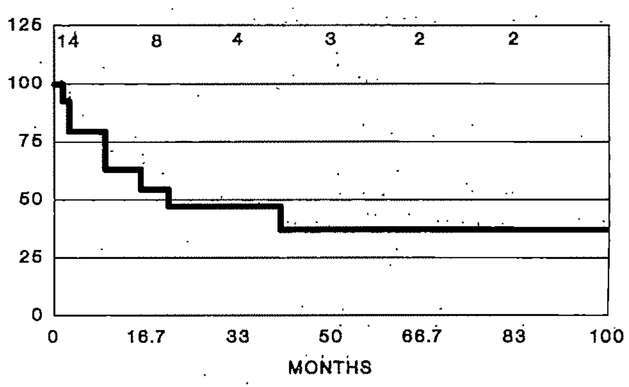

Fig 1. Actuarial survival for 14 patients with supradiaphragmatic extension of vena caval tumor thrombus.

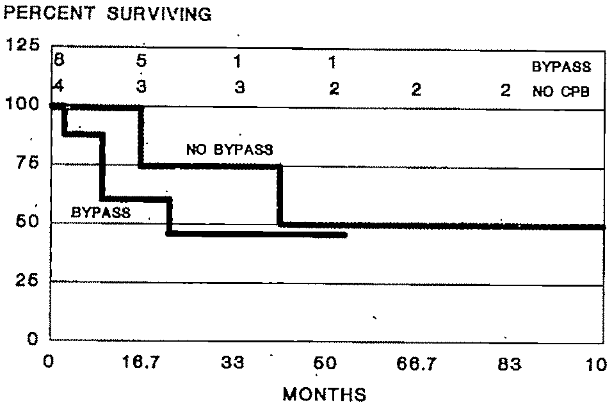

Fig 2. Actuarial survival of 12 patients after resection of tumor thrombus with (group C) and without (group B) cardiopulmonary bypass (CPB).

patient numbers are small, one half of patients are alive 4 and 5 years after cavoatrial tumor thrombectomy for disease that has extended above the diaphragm. Median survival after tumor thrombectomy with cardiopulmonary bypass is 17 months, and after excision without bypass it is 41 months. Survival differences between groups are not significant ($p = 0.43$). Actuarial survival based on stage of disease at operation is presented in Figure 3. For stage III disease survival is 100% at 1 year and 83% (CL, 98% and 68%) at 3 and 5 years. Survival for stage IV disease is 29% (CL, 46% and 12%) at 1 year and 14% (CL, 27% and 1%) at 3 years, with no patient surviving past 41 months. Postoperative survival is related closely to stage of disease at operation rather than operative approach. Median survival has not yet been reached in patients with stage III disease, and is 6 months with stage IV disease. Survival in these two groups is statistically different ($p = 0.002$; Gehan's and Peto's Wilcoxon test, NCSS).

Comment

It has been well established that renal cell carcinoma with tumor propagation into the vena cava responds favorably to excision in the absence of extensive nodal or distant metastases. Previous techniques to isolate and excise tumor that has extended above the diaphragm have included venovenous shunting, vascular isolation with cross-clamping of the abdominal aorta, balloon catheter retrieval, cardiopulmonary bypass, and hypothermic circulatory arrest [1–8, 10–13]. Although circulatory arrest allows bloodless visualization of the vena caval tumor thrombus, it is accompanied by serious perioperative morbidity and mortality.

Comparison of the results in the present series with those of similar contemporary techniques using profound hypothermia and circulatory arrest is complicated by the fact that many series have included all patients with transluminal propagation of renal and adrenal tumors. Complications, hospital stay, and survival statistics are not presented in a uniform fashion, and patients have not been stratified according to American Joint Committee on Cancer staging guidelines. Reviewing the published series, perioperative mortality rates range from 0% to 33%. We experienced no operative mortality in the small number of patients in the present series. Perfusion time in our experience has averaged 72 minutes, with no patient requiring longer than 95 minutes. Few series have published the duration of cardiopulmonary bypass required to accomplish tumor excision with circulatory arrest. Using accepted guidelines of cooling at a rate of no more than 1°C per minute and rewarming no faster than 0.5°C per minute, to cool and rewarm to 20°C requires at least 1 hour of bypass time. The addition of another 45 to 60 minutes to allow for tumor removal extends pump time to 2 hours. In a recent review, bypass time averaged 136 minutes [4].

Transfusion requirements are greater in reported series using circulatory arrest to remove tumors with extension above the diaphragm [4, 6, 7]. Potential concerns regarding the autotransfusion of blood shed during this operation have not been borne out in our experience. Given the massive numbers of tumor cells that these intravascular tumors shed into the vasculature daily, aspiration of blood at the time of operation should present no additional risk. Substantial survival 4 years postoperatively in stage III patients in this series would seem to substantiate this concept.

Perioperative renal and hepatic failure has occurred in several series of patients operated on with circulatory arrest [4, 8]. Sepsis has been reported frequently in these patients postoperatively and may be related to translocation of bacteria from the intestine [4]. In no patient in the present series did renal failure, hepatic failure, sepsis, cerebrovascular accident, myocardial infarction, or pulmonary embolus develop.

There appear to be few 5-year survivors reported after resection of tumors that have propagated above the diaphragm (Table 3). Survival in this series approximates results achieved in patients after complete excision when the intravascular tumor is confined to the infrahepatic IVC.

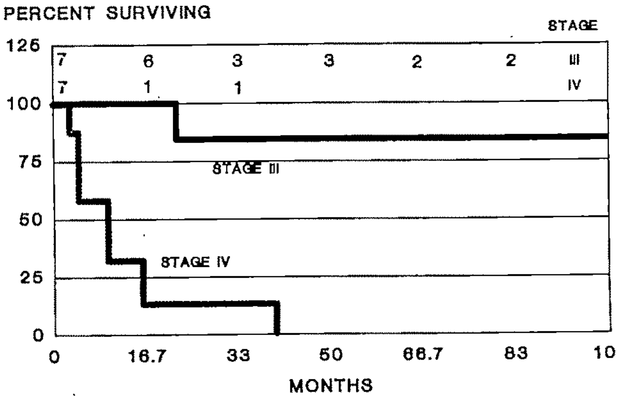

Fig 3. Actuarial survival based on pathologic stage of renal and adrenal tumors at time of resection (stage III and stage IV).

Table 3. Postoperative Cavoatrial Tumor Survival

Series	Year	Median Survival Time (mo)	5-Year Survivors (No.)
Novick et al [7]	1990	24	0
Skinner et al [13]	1989	?	0
Marshall et al [4]	1988	14.8	0
Shahian et al [6]	1990	Not yet reached	0
Sosa et al [3]	1984	13	1
Present series	1991	18.5	1

Conclusions and Recommendations

With the survival data as presented, it appears reasonable to pursue an aggressive approach to the management of patients with vena caval extension of their renal or adrenal tumor that propagates above the diaphragm, in the absence of extensive metastatic disease. If extraction of the tumor thrombus can be accomplished completely and safely without high-dose systemic heparin administration and cardiopulmonary bypass, this should be encouraged. Although some authors advocate the routine use of deep hypothermia and circulatory arrest for removal of caval tumor thrombi, the risks involved do not seem justified given our experience with tumor thrombectomy on cardiopulmonary bypass. In contrast to the opinion expressed by some, tumor thrombus is rarely invasive or densely adherent to the vena cava and right atrium and it is readily excised using bypass alone in most cases. In our opinion, circulatory arrest should be reserved for those patients in whom adequate visualization of the tumor for thrombectomy, or resection and replacement of the IVC, cannot be achieved otherwise.

References

1. Marshall V, Middleton RG, Holswade GR, et al. Surgery for renal cell carcinoma in the vena cava. J Urol 1970;103:414–20.
2. Skinner D, Pfister R, Colvin R. Extension of renal cell carcinoma into the vena cava: the rationale for aggressive surgical management. J Urol 1972;107:711–6.
3. Sosa RE, Muecke EC, Vaughan ED, et al. Renal cell carcinoma extending into the inferior vena cava: the prognostic significance of the level of vena caval involvement. J Urol 1984;132:1097–100.
4. Marshall FF, Dietrick DD, Baumgartner WA, Reitz BA. Surgical management of renal cell carcinoma with intracaval neoplastic extension above the hepatic veins. J Urol 1988;139:1166–72.
5. Utley JR, Mobbin-Uddin K, Segnitz RH, Belin RP, Utley JF. Acute obstruction of tricuspid valve by Wilms' tumor. J Thorac Cardiovasc Surg 1973;66:626–8.
6. Shahian DM, Libertino JA, Zinman LN, Leonardi HK, Eyre RC. Resection of cavoatrial renal cell carcinoma employing total circulatory arrest. Arch Surg 1990;125:727–32.
7. Novick AC, Kaye MC, Cosgrove DM, et al. Experience with cardiopulmonary bypass and deep hypothermic circulatory arrest in the management of retroperitoneal tumors with large vena caval thrombi. Ann Surg 1990;212:472–7.
8. Prager RL, Dean R, Turner B. Surgical approach to intracardiac renal cell carcinoma. Ann Thorac Surg 1982;33:74–7.
9. Kambam J, Meszaros R, Merrill W, Stewart J, Smith BE, Bender H. Prophylactic administration of histamine$_1$ and histamine$_2$ receptor blockers in the prevention of protamine related haemodynamic effects. Can J Anesth 1990;37:420–2.
10. Paul JG, Rhodes DB, Skow JR. Renal cell carcinoma presenting as right atrial tumor with successful removal using cardiopulmonary bypass. Ann Surg 1975;181:471–3.
11. Novick AC, Cosgrove DM. Surgical approach for removal of renal cell carcinoma extending into the vena cava and the right atrium. J Urol 1980;123:947–50.
12. Libertino JA, Zinman L, Watkins E. Long-term results of resection of renal cell cancer with extension into inferior vena cava. J Urol 1987;137:21–4.
13. Skinner DG, Pritchett TR, Lieskovsky G, Boyd SD. Stiles QR. Vena caval involvement by renal cell carcinoma. Ann Surg 1989;210:387–94.

DISCUSSION

DR HARVEY I. PASS (Bethesda, MD): This is really a nice series. I just have a quick philosophical question. What do you do for the patient who has caval disease with or without supradiaphragmatic extension when you see the computed tomographic scan and you are worried about two or three pulmonary nodules? Do you approach that patient the same way? I suppose this will tie in with alternative therapies you have available at Vanderbilt at this time for this poor-risk group of patients.

DR STEWART: Yes, we would approach the patient the same way and would perform pulmonary metastasectomy. Before evaluating our series we really had no idea of how well the stage IV patients would do, but still we think that the survival may be somewhat improved after resection in these patients. This is a good form of palliation.

We have had recent success in a very limited number of patients using outpatient, oral etoposide therapy in patients with metastatic renal cell carcinoma. Our experience is somewhat encouraging, but the data are far too preliminary to present anything at this time.

DR MICHAEL D. HOROWITZ (Miami, FL): In the last 2 years, I had the opportunity to operate on 3 of these patients. For the first 2 we did not use perfusion. For the most recent 1, which was last week, we used perfusion and circulatory arrest. I would like to make a few points.

I concur completely with your use of some method of vena caval interruption. Our second patient died at home of a pulmonary embolus 8 weeks after an otherwise curative operation. These patients have tremendous venous-system pathology and I think there certainly is a substantial risk for pulmonary embolus.

The other point I would like to make relates to the problem of tumor embolization. In our most recent patient, in whom we used perfusion and circulatory arrest, the perfusionist noted bits of tumor within the venous reservoir during the cooling period. He changed the reservoir during the 24-minute period of circulatory arrest. Have you noticed this, and do you have any feelings as to whether this is oncologically important? Of course, these people all have preexisting tumor within the vasculature. If this tumor embolization is due to the initial mobilization of the kidney, it is likely that this patient would have had a major pulmonary embolus had we not been on bypass at the time.

DR STEWART: We have been very concerned about both of those problems, and with manipulation of the kidney and vena cava. We work very hard to try to minimize manipulation of the vena cava during the nephrectomy or adrenalectomy. When the tumor extends above the diaphragm we put an umbilical tape around the intrapericardial vena cava and work very hard to minimize any manipulation of the IVC or the right atrium at that point. We use a right-angled metal-tipped cannula to cannulate the superior vena cava to avoid any kind of intervention into the right atrial cavity itself that might promote embolization of the tumor.

We have not noticed any tumor fragments within the bypass circuit. Obviously, when one uses a cardiotomy suction one is going to be aspirating tumor cells. Although initially we believed that was very important, it seems to be less so based on our more recent results with short-term survival. Some people have estimated that there are millions of cells released on a daily basis within the vasculature—I do not have any definitive data on that, however.

DR ALLAN L. GRAHAM (Fort Worth, TX): I have one question and one comment. Do you have any suggestion for the patient in whom you find the tumor thrombus is friable but stuck to the IVC and you have a difficult time getting it loose from the wall?

The comment is that one of the patients we had was having difficulty with the IVC catheter draining well. It was inserted from the femoral vein to the bifurcation of the IVC. When it was removed, there was tumor thrombus in the catheter itself.

DR STEWART: To avoid either thromboembolus or tumor thrombus from getting into the venous drainage, we have routinely performed—if we are going to femoral cannulation, for instance—venous thrombectomy before we initiate bypass to make certain that there was not extension of thrombus. By and large we can determine this preoperatively using the magnetic resonance imaging scan. Magnetic resonance imaging provides very nice pictures of both coronal, sagittal, and axial planes of the vena cava, and we can differentiate often the difference between tumor thrombus and propagation of thrombus in an occluded vena cava. We generally have this information ahead of time and we know to which level the thrombus extends, how far to put the cannula in, where best to cannulate, and where to occlude the cava proximally.

It should be noted that the tumor thrombus is often adherent to the caval wall, but rarely invasive. One can usually achieve a clean resection by removing the tumor thrombus using endarterectomy instruments. If the tumor is very friable, we have not hesitated to remove it in a piece-meal fashion.

Notice From the Southern Thoracic Surgical Association

The Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Grand Cypress, Orlando, Florida, November 7–9, 1991. There will be a $250 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 7, 1991. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Members wishing to participate in the Scientific Program should submit an original abstract and one copy by May 15, 1991, to Frederick L. Grover, MD, Program Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267. Abstracts must be submitted on the Southern Thoracic Surgical Association abstract submission form. These forms may be obtained from the Association's office or in the April issue of *The Annals of Thoracic Surgery*. All slides used during the presentation must be 35 mm. Manuscripts of accepted papers must be submitted to *The Annals of Thoracic Surgery* prior to the 1991 meeting or to the Secretary-Treasurer at the opening of the Scientific Session.

Applications for membership should be completed by July 1, 1991, and forwarded to F. Hammond Cole, Jr, MD, Membership Committee Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267.

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Temporary External DDD Pacing After Cardiac Operations

T. Bruce Ferguson, Jr, MD, and James L. Cox, MD

Division of Cardiothoracic Surgery, Washington University School of Medicine, St. Louis, Missouri

Temporary atrial and ventricular pacing in the DVI, VVI, and AOO modes using atrioventricular sequential DVI devices is routinely used in cardiac operations. This study evaluated a new temporary external DDD pacemaker (Medtronic 5345 External Pulse Generator) capable of ten pacing modes. Thirty-nine devices have been applied to 38 adult patients (27 male, 11 female) after a variety of open heart procedures. Group 1 had atrial pacing wires placed 1.5 to 2.0 cm apart superiorly on the right atrium, group 2 had atrial wires placed 1.0 to 1.5 cm apart on the right atrial free wall, and group 3 had atrial wires placed on the right atrial free wall 0.8 cm apart, using a Silastic ring for fixation. Ventricular wires were placed on the free wall (group 1) or the diaphragmatic surface (groups 2 and 3) of the right ventricle. Postoperative atrial and ventricular sensing and pacing thresholds were obtained on return to the intensive care unit; analysis of variance demonstrated a significantly greater atrial sensing threshold in group 3. Four patients in group 1 permanently lost atrial sensing, 1 patient in group 2 intermittently lost atrial sensing at 24 hours with return at 36 hours postoperatively, and 1 patient in group 1 lost ventricular sensing capability. All other patients had adequate atrial and ventricular sensing capability documented until elective pacemaker removal (mean, 166 hours; range, 17 to 667.5 hours). Nineteen patients required some form of temporary pacing postoperatively; 11 patients demonstrated hemodynamic benefit from a pacing mode that is not available on the currently used DVI devices, and 7 of these required true DDD pacing capability. Six patients benefited from atrial pacing with adequate atrial sensing and simultaneous ventricular backup. Burst pacing with the device was used successfully to treat postoperative atrial flutter in 2 patients. We conclude that temporary external DDD pacing is feasible and effective in postoperative cardiac surgical patients. Atrial sensing is possible in most patients but electrode positioning is important for adequate thresholds. In some patients, hemodynamic as well as electrophysiologic improvement can be demonstrated with universal DDD pacing capability as compared with standard DVI pacing.

(Ann Thorac Surg 1991;51:723–32)

Temporary external pacing has been available in various forms for the past 24 years. Harris and associates [1] first described epicardial pacing to control bradyarrhythmias after cardiac operations. Work by Waldo and colleagues [2–4] extended these techniques to the diagnosis and treatment of atrial arrhythmias in postoperative patients. At the same time, dual-chamber pacemakers became available for permanent implantation, and a great deal of experience in nonsurgical patients was acquired. Gradually, this technology was applied to post–myocardial infarction and postsurgical patients by the use of temporary atrioventricular (AV) sequential (DVI) pacemakers. The hemodynamic benefits of this mode of pacing were demonstrated by Chamberlain and co-workers [5] in patients with heart block after acute myocardial infarction, and Fields and associates [6] described the initial experience with temporary AV sequential pacing in postoperative cardiac patients. Hartzler and colleagues [7] compared the hemodynamic effects of ventricular, atrial, and AV sequential pacing after cardiac operations, demonstrating the superiority of AV sequential pacing over the other two modes under most circumstances. At the beginning of the past decade Waldo and MacLean [8] documented the efficacy in virtually all patients of temporary external pacing after cardiac operations and recommended that temporary wires be placed on both the atrium and ventricle in every patient after surgical intervention.

Thus for the past 10 years, routine temporary postoperative pacing techniques have been used by a majority of cardiothoracic surgeons. The most commonly used pacing modes have been atrial asynchronous pacing (AOO), AV sequential pacing (DVI), and ventricular inhibited pacing (VVI). Concomitant atrial inhibited pacing (AAI) with ventricular backup (VVI) required two separate pacemakers (one single-chamber device attached to each pair of leads). The AV sequential devices used during this time were only capable of atrial asynchronous pacing because an atrial sensing circuit was not incorporated into them.

In the early part of the past decade, permanent, transvenous, universal DDD pacemaker devices became available, and considerable experience has now been acquired with these devices in patients requiring permanent pacing [9]. The difference between DVI and DDD pacing is

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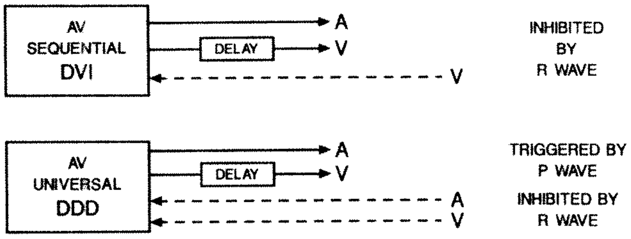

Fig 1. Schematic diagram of temporary DVI and DDD pulse generators. Both devices contain atrial pacing circuits, programmable atrioventricular (AV) delay, and ventricular pacing circuitry that is inhibited by the patient's R wave. DDD pacemakers contain in addition circuitry for atrial sensing, such that the device can be triggered by the patient's own P wave. (A = atrium; V = ventricle.)

illustrated in Figure 1. Potential problems with *external* DDD pacing in the setting of postoperative cardiac surgery include (1) the more complicated atrial sensing circuitry and electrogram recording parameters required for DDD pacing, (2) the increased electrophysiologic sophistication required to program the devices, and (3) the more complicated electrocardiographic interpretations occasionally necessary with DDD pacing. Nevertheless, Littleford and associates [10] in 1984 described the initial application of a temporary DDD pacing unit using temporary transvenous wires. Billhardt [11], Haffajee [12], and Hauser and Vicari [13] have all addressed the potential benefits of external DDD pacing in postoperative cardiac surgical patients in recent reviews on temporary pacing. The ability to provide (1) a "universal" pacing mode capable of atrial or ventricular chamber pacing or both without reprogramming and (2) P wave sensed ventricular pacing were predicted to be of benefit in postoperative patients.

Recently, Wallenhaupt and Rogers [14] have reported on the intraoperative use of a modified explanted DDD pacemaker in 2 patients after open heart operations with demonstrated hemodynamic benefit. This report will present our initial experience with a new, external DDD pulse generator capable of ten pacing modes, burst pacing capability, and histogram storage and analysis.

Material and Methods

The external DDD pulse generator (Medtronic Model 5345 Pulse Generator; Medtronic, Inc, Minneapolis, MN) was applied to 38 patients in this study. Informed consent was obtained before application in accordance with the guidelines of the Human Studies Committee at Washington University.

The device is capable of ten pacing modes and is designed for use with temporary myocardial or transvenous lead systems. Programmable features include atrial and ventricular rate, output, pulse width, and sensing threshold, along with the atrial refractory period and AV interval. The generator contains a safety pacing feature that prevents inappropriate inhibition of ventricular pacing caused by far-field sensing (crosstalk) and automatic extension of the atrial refractory period after a sensed premature ventricular contraction to decrease the possibility of pacemaker-mediated tachycardia.

After completion of the operative procedure and while the patient was still on cardiopulmonary bypass, temporary atrial and ventricular pacing wires were placed on each patient. One pair of wires was placed on the atrium and ventricle, respectively. Two different types of temporary atrial pacing wires were examined in the study (Ethicon TPW-30 temporary heart wires; Ethicon, Inc, Somerville, NJ; and Medtronic 6500 temporary heartwires; Medtronic Inc). One type of ventricular wire was used in all patients (Medtronic 6500 temporary heart wires; Medtronic Inc).

Electrode placement reflected the preferences of the surgeon at the commencement of the study. The atrial wires were placed either near the right atrial appendage or on the right atrial free wall; the ventricular wires were placed on the right ventricular free wall or on the diaphragmatic surface of the right ventricle. Group 1 patients (N = 13) had Ethicon wires placed near the right atrial appendage, spaced 1.5 to 2.0 cm apart (Fig 2). Group 2 patients (N = 13) had Ethicon wires placed on the right atrial free wall, spaced 1.0 to 1.5 cm apart (Fig 3). Group 3 patients (N = 12) had Medtronic 6500 wires placed on the right atrial free wall with the interelectrode distance fixed at 0.8 cm with a Silastic button (Fig 4). One patient in group 1 had a second set of atrial wires placed on the left atrial appendage as well. All group 1 patients had Medtronic 6500 wires placed on the free wall of the right ventricle; the remaining patients had Medtronic 6500 wires placed on the diaphragmatic surface of the right ventricle just beneath the acute margin of the heart.

After exteriorization of the temporary leads and connection to the Model 5345 generator, pacing capability was confirmed before termination of cardiopulmonary bypass. If temporary pacing was necessary to terminate bypass or to optimize hemodynamic performance, the appropriate pacing mode was programmed.

For the total of 38 patients, all but two of the surgical procedures were performed using cardioplegic arrest with crystalloid cardioplegic solutions. These two included the cryosurgical procedure for AV node reentry tachycardia, which was performed at 37°C on cardiopulmonary bypass, and the exploration for right ventricular perforation, which did not require bypass.

After return to the cardiac intensive care unit demographic, cardiac historical, and preoperative drug therapy data were acquired from the medical record. Atrial and ventricular pacing and sensing thresholds were determined using the 5345 generator. The devices were programmed according to the hemodynamic and electrophysiologic requirements of the patients; if temporary pacing was not required then the devices were programmed into the DDD mode with a lower rate approximately 20 beats per minute (bpm) below the intrinsic sinus rate, upper rate of 120 bpm, atrial and ventricular outputs 10 to 20 mA, atrial and ventricular pulse widths 1.0 ms, and bipolar polarity. Sensitivity parameters, AV intervals, and atrial refractory periods were individually

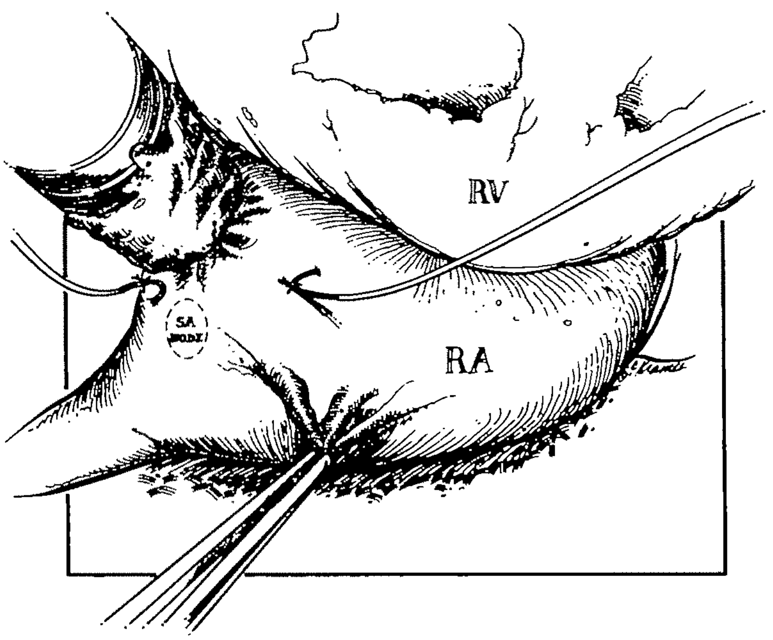

Fig 2. Location of temporary atrial pacing bipolar wires on the right atrium near the atrial appendage, as positioned in group 1 in the study. Interelectrode distance varied between 1.5 and 2.0 cm. The location of the SA node is illustrated. (RA = *right atrium;* RV = *right ventricle.)*

programmed. All programmed data were recorded every 8-hour nursing shift and at the time of reprogramming of the generator for the duration of the application of the device. All pacing events and complications were completely evaluated and documented with hard-copy electrocardiograms recorded from the intensive care unit monitoring system.

Postoperative supraventricular arrhythmias (premature atrial contractions, atrial flutter, atrial fibrillation) were documented with unipolar and bipolar atrial electrograms and treated with rapid atrial pacing, pharmacologic therapy, or both.

The devices were maintained in the DDD mode until removal; diagnostic information of intrinsic electrical activity and paced activity were recorded on a daily basis and displayed in histogram form until termination of the device. The reason for discontinuation of the devices included (1) loss of adequate sensing, (2) elective removal in patients not requiring pacing to apply the device to another patient, and (3) elective removal to remove the temporary pacing wires. The reason was documented in all patients.

After completion of the study, the temporary wires were removed in the usual fashion.

Statistical analysis for sensing and pacing thresholds was performed by univariate analysis using the SYSTAT

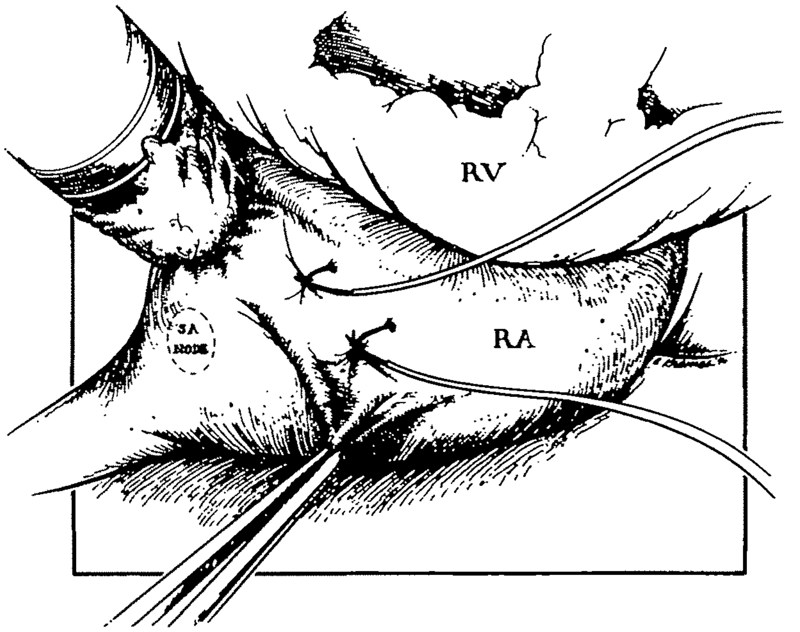

Fig 3. Location of temporary atrial pacing bipolar wires on the right atrial free wall, as positioned in group 2 in the study. Interelectrode distance varied between 1.0 and 1.5 cm. (RA = *right atrium;* RV = *right ventricle.)*

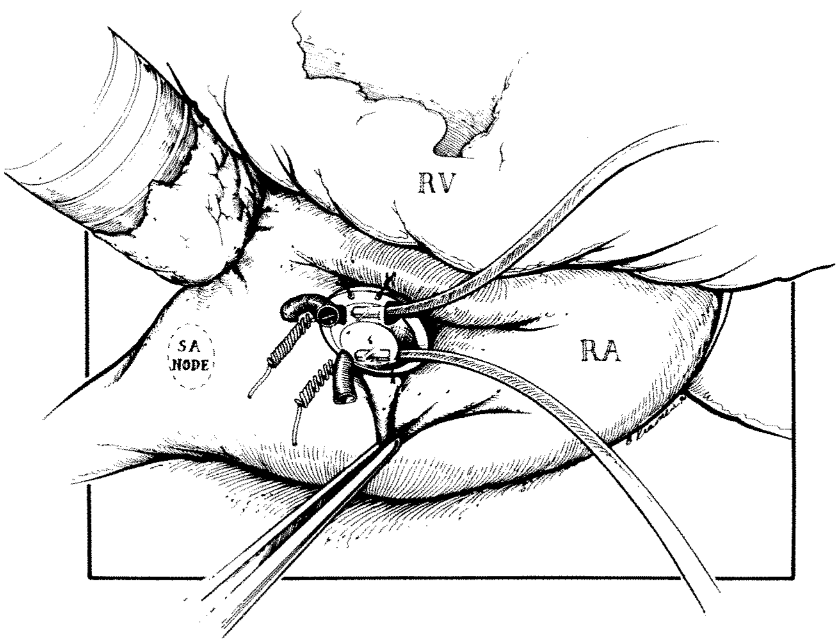

Fig 4. Location of temporary atrial pacing bead electrodes on the right atrial free wall, as positioned in group 3 in the study. Interelectrode distance was fixed at 0.8 cm by the Silastic ring. (RA = *right atrium;* RV = *right ventricle.)*

(Systat, Inc, Chicago, IL) software statistical analysis package. Data are expressed as mean ± standard deviation.

Results

The 38 patients underwent a total of 39 applications of the device. Table 1 lists the patient demographic and preoperative variables and the type of surgical procedure performed. The large percentage of arrhythmia cases reflects our surgical practice at Washington University. The patient undergoing the left atrial isolation procedure for ectopic atrial tachycardia had two simultaneous applications of the device.

Table 1. Condition and Operation in 38 Patients[a] *(39 applications)*

Condition	Operation	No. of Patients
CAD	CABG	20
CAD, aneurysm	CABG/LVA	1
AS, CAD	CABG/AVR	1
Ischemic MR	CABG/MVR	1
AS	AVR	1
RV perforation	Sternotomy	1
WPW	Endocardial division	7
AVN reentry	Discrete cryosurgery	1
Atrial fibrillation	MAZE procedure	2
Ectopic atrial T	Left atrial isolation	1
Ventricular T	CABG/EER + cryo	1
	CABG/AICD	1

[a] There were 27 male and 11 female patients.

AICD = automatic implantable cardioverter-defibrillator; S = aortic stenosis; AVN = atrioventricular nodal reentry tachycardia; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CAD = coronary artery disease; EER + cryo = extended endocardial resection plus cryosurgery for ventricular tachycardia; LVA = left ventricular aneurysmectomy; MR = mitral regurgitation; MVR = mitral valve replacement; RV = right ventricular; T = tachycardia; WPW = Wolff-Parkinson-White syndrome.

Figures 5 and 6 illustrate data obtained in the operating room after termination of cardiopulmonary bypass. Figure 5 demonstrates adequate atrial tracking of the patient's own sinus rhythm. The pulse generator was programmed to the DDD mode with a lower rate equal to the patient's own sinus rate. When the sinus rate drops below the lower rate of the pacemaker, the patient's atrium is paced; when the sinus rate speeds up and exceeds the programmed rate, adequate atrial and ventricular sensing are demonstrated and a normal sinus depolarization occurs. Atrioventricular conduction is intact throughout, and there are no hemodynamic alterations that result from the change to atrial sensing from atrial pacing.

Figure 6 illustrates the same hemodynamic and electrophysiologic parameters as in Figure 5. These data were taken from a patient after aortic valve replacement in whom transient AV conduction delay was present postoperatively. Effective P wave sensed ventricular pacing (VDD mode) is demonstrated. The patient's sinus rhythm is adequately sensed by the device, with subsequent ventricular pacing at a programmed AV delay of 180 ms. There was moderate hemodynamic improvement with VDD pacing as opposed to DVI pacing in this patient.

Table 2 lists the sensing and pacing threshold data by group. The group 3 patients had a significantly greater atrial sensing threshold than did groups 1 or 2 by univariate analysis. Placement of the ventricular wires on the diaphragmatic surface of the right ventricle (groups 2 and 3) resulted in greater ventricular sensing thresholds than did placement on the right ventricular free wall, but this difference was not significant. Placement of the atrial

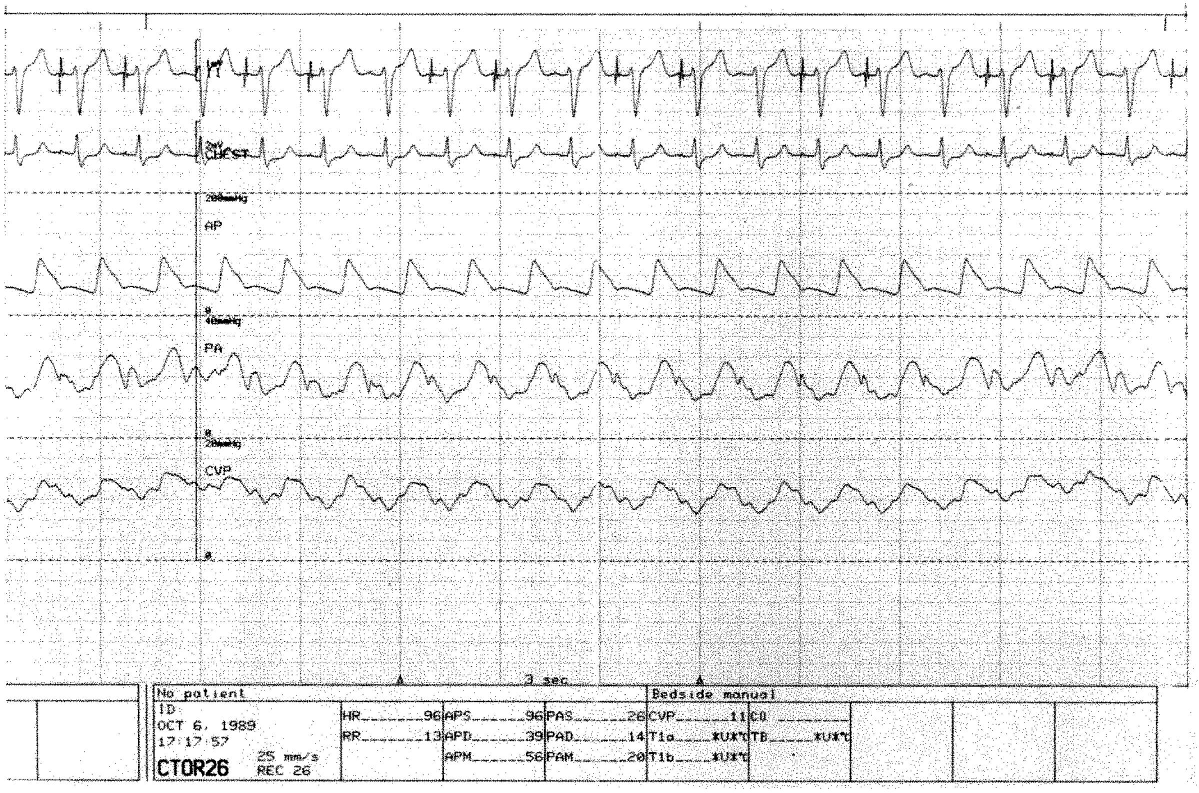

Fig 5. Intraoperative electrophysiologic and hemodynamic data obtained after termination of cardiopulmonary bypass. Adequate atrial tracking of the patient's own sinus rhythm is illustrated. The pulse generator was programmed into the DDD mode with a lower rate approximately equal to the patient's own sinus rate. When the sinus rate drops below the lower rate of the pacemaker, the patient's atrium is paced; when the sinus rate speeds up and exceeds the programmed rate, adequate atrial and ventricular sensing are demonstrated and a normal sinus depolarization occurs. Atrioventricular conduction is intact throughout, and there are no hemodynamic alterations that result from the change to atrial sensing from atrial pacing. (AP = *radial arterial pressure;* CHEST = *chest electrocardiographic lead;* CVP = *central venous pressure;* PA = *pulmonary artery pressure;* II = *surface electrocardiographic limb-lead II.*)

electrodes on the free wall resulted in lower pacing thresholds than placement near the atrial appendage, but again these differences were not significant.

Table 3 lists the postoperative sensing data. Atrial sensing capability was lost permanently in 4 patients in group 1 and temporarily in 1 patient in group 2. In this patient, adequate sensing was lost at 24 hours but returned at 36 hours. No patients in group 3 lost atrial sensing capability throughout the duration of application of the devices. When adequate sensing capability was lost, however, the usefulness of the 5345 device as compared with the DVI devices was no longer present and the 5345 generator was reprogrammed to a standard postoperative pacing mode (eg, VVI for backup) or discontinued. One patient in group 1 lost ventricular sensing capability at 17 hours. The reason for this was unclear.

Twenty of 38 patients required some form of temporary pacing during the postoperative period (Table 4). Most commonly, DDD pacing was used postoperatively for hemodynamic or electrophysiologic reasons. With adequate atrial sensing, all of the *effective* modes of AAI or VDD in addition to true DDD pacing could be accomplished by programming the generators to the universal DDD mode. These are pacing modes that are not available with the currently used DVI devices.

Eleven patients in the group requiring pacing demonstrated some type of hemodynamic benefit from use of a pacing mode that is not available with the DVI devices. Four of these patients had an intact sinus node and temporary prolongation of AV conduction postoperatively; effective VDD pacing was used in these patients until AV conduction returned to normal. Two additional patients had heart block and sinus bradycardia and required DDD pacing. The remaining 5 patients benefited from DDD pacing as recovery of normal sinus node function occurred over time in patients with junctional rhythms (2 patients), atrial quiescence (1 patient), and sinus bradycardia (2 patients).

Six patients requiring pacing had temporary augmentation of their sinus rate in the postoperative period. The advantage of atrial sensing capability in this setting is demonstrated in Figure 7. The patient had a history of premature atrial contractions (PACs) and underwent redo coronary artery bypass grafting. In the immediate postoperative period data in sinus rhythm, AOO, and effective AAI pacing demonstrated the need for an increase in sinus rate for hemodynamic reasons. Attempts to overdrive capture the atria were unsuccessful, with atrial pacing spikes occurring throughout the cardiac cycle owing to the PACs. With adequate effective pacing in the

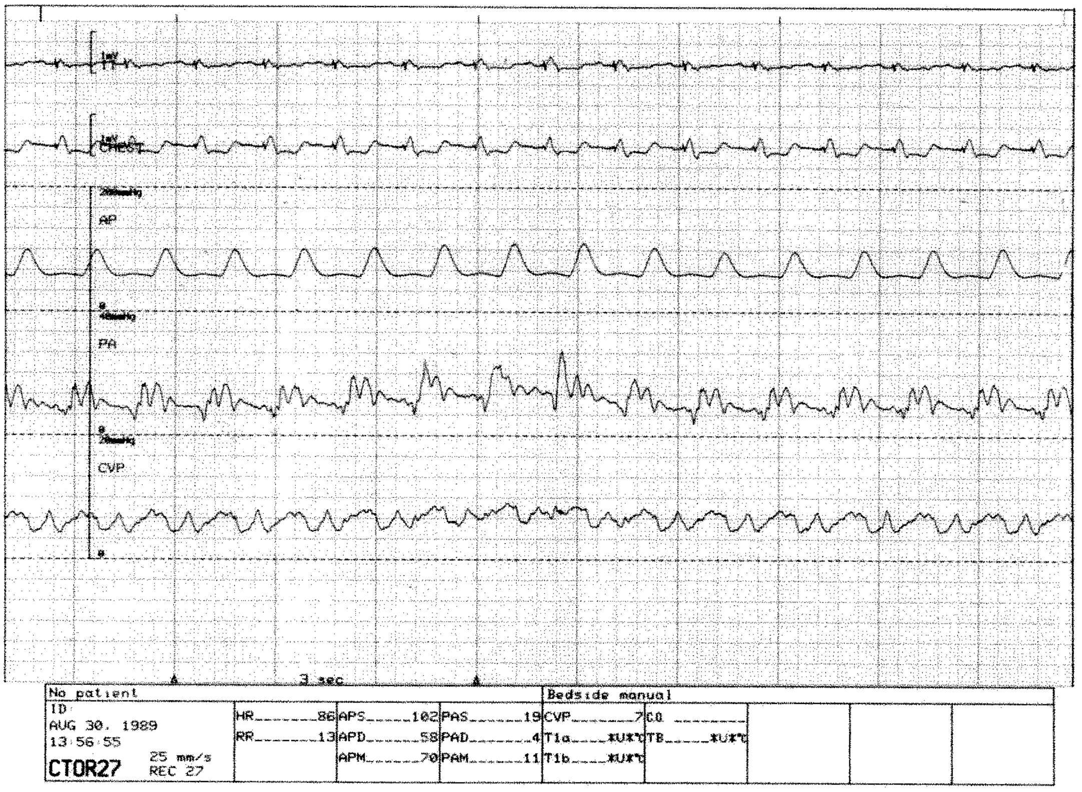

Fig 6. Data taken from a patient after termination of bypass following aortic valve replacement in whom transient atrioventricular conduction delay was present. Effective P wave triggered ventricular pacing (VDD mode) is demonstrated with the device programmed in the DDD mode. The patient's sinus rhythm is adequately sensed by the device, with each sinus depolarization followed by ventricular pacing at a programmed atrioventricular delay of 180 ms. There was moderate hemodynamic improvement with VDD as opposed to DVI pacing in this patient. (Abbreviations are the same as in Figure 5.)

AAI mode, a modest hemodynamic improvement was demonstrated owing to the increased sinus rate but with appropriate sensing of the PACs.

Each device was applied in a continuous fashion until removal; mean duration of application for the entire group was 166 ± 13.7 hours (range, 17 to 667.5 hours) (Table 5). Once temporary pacing (in a mode other than the DDD mode) was no longer necessary the devices were reprogrammed into the DDD mode at a lower rate of 60 bpm, upper rate of 120 bpm, atrial refractory period of 250 ms, AV interval of 180 ms, A sense of 0.5 mV, and V sense of 1.0 mV. If patients did not require temporary pacing postoperatively, the devices were programmed to these parameters after return to the intensive care unit. As indicated in Table 5, 3 of the 5 patients who lost atrial sensing capability lost it within the first 96 hours postoperatively. In the majority of patients, atrial sensing thresholds remained stable throughout the perioperative period.

The 1 patient with two simultaneous applications of the device had undergone a left atrial isolation procedure. Postoperatively, the first device was connected to the right and left atria through the atrial and ventricular channels; the device was programmed into the DDD mode with a programmed 40-ms delay to mimic normal atrial depolarization time. The isolated left atrial tissue was paced with the device for the first 4 days postoperatively until the patient's ectopic tachycardia intermittently returned. The second device was connected to wires on the right atrium and ventricle, respectively, and programmed into the VDD mode to track the first pacemaker. The patient had a modest improvement in hemodynamic performance by shortening the AV interval from an in-

Table 2. Sensing and Pacing Threshold Data

Group	N	A Sense (mV)	V Sense (mV)	A Pace (mA)	V Pace (mA)
1	13	0.97 ± 0.79	6.50 ± 3.80	3.21 ± 2.70	1.14 ± 0.97
2	13	1.99 ± 0.99	8.24 ± 3.48	2.15 ± 0.46	1.21 ± 0.40
3	12	5.07 ± 1.41[a]	8.79 ± 3.53	1.66 ± 0.37	1.10 ± 0.32

[a] $p < 0.05$, 3 versus 1 and 2, analysis of variance.

Table 3. Postoperative Sensing Data

Loss of Sensing	Operation	Hours Postop at Time of Loss	Postop Pacing Required
Atrial			
Group 1 (4 patients)	CABG/LVA	17	Y
	CABG	45	Y
	CABG	123	N
	CABG/AVR	68	Y
Group 2			
(1 patient [intermittent])	CABG/VT	24	Y
Ventricular			
Group 1 (1 patient)	CABG	23	N

AVR = aortic valve replacement; CABG = coronary artery bypass grafting; LVA = left ventricular aneurysmectomy; VT = endocardial resection and cryosurgery for ventricular tachycardia.

trinsic value of 200 ms to a programmed 150 ms for the first 12 hours postoperatively. Thereafter the patient's hemodynamic status, with or without the presence of the tachycardia in the isolated left atrial tissue, was excellent.

Table 4. Postoperative Pacing

Operation	Indication	Mode Programmed (Effective Mode)
MAZE	SB	DDD
CABG	SB	DDD (AAI)
CABG	SB	DDD (AAI)
CABG	SB	DDD (AAI)
CABG	SB	DDD
Close RV perforation	SB	DDD (AAI)
CABG	SB	DDD (AAI)
CABG (redo)	SB, PAC	DDD (AAI)
CABG/LVA	AVB	DDD (VDD)
AVR	Int AVB	DDD (VDD)
CABG	2°AVB	DDD (VDD)
CABG/MVR	AVB	DDD
CABG/AICD	Int AVB	DDD (VDD)
CABG/AVR	Int AVB, SSS	DDD
MAZE	Junct, SSS	DDD
WPW	Junct	DDD
LAI	Atrial quiescence	DDD, VDD[a]
CABG/VT	Flutter	RAP
AVNR	Flutter	RAP
CABG/AICD	Flutter	RAP

[a] Simultaneous application of two devices.

AICD = automatic implantable cardioverter-defibrillator; AVB = atrioventricular block; AVNR = discrete cryosurgical procedure for atrioventricular nodal reentrant tachycardia; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; Int = intermittent; Junct = junctional rhythm; LAI = left atrial isolation procedure for ectopic atrial tachycardia; MVR = mitral valve replacement; PAC = premature atrial contractions; RAP = rapid atrial pacing (Medtronic 5345 device); RV = right ventricular; SB = sinus bradycardia; SSS = sick sinus syndrome; VT = endocardial resection + cryosurgery for ventricular tachycardia; WPW = ablation for Wolff-Parkinson-White syndrome; 2° = second degree.

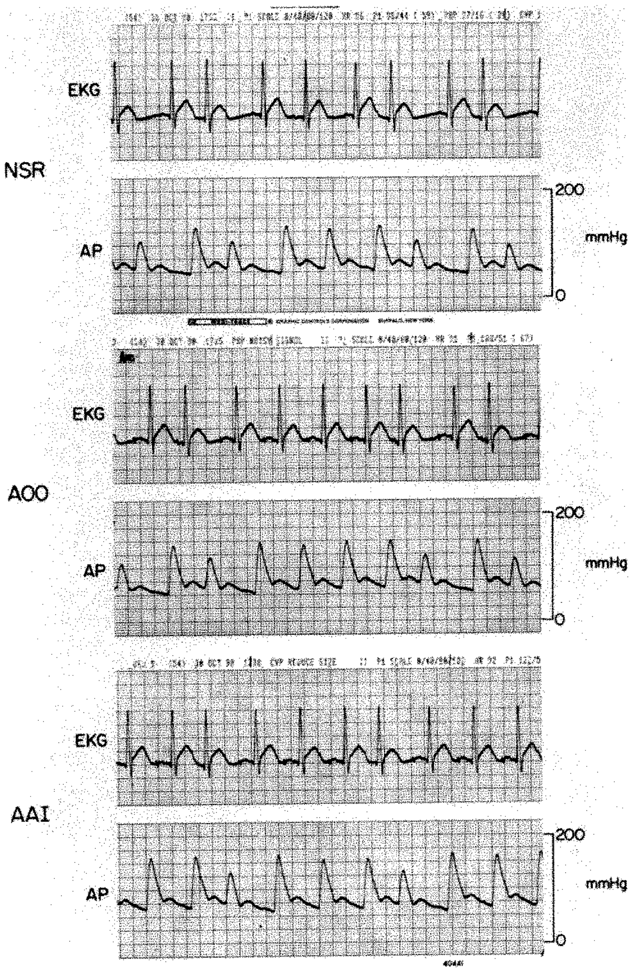

Fig 7. Data obtained in the intensive care unit from a patient with a history of premature atrial contractions who had undergone redo coronary artery bypass grafting. Electrocardiographic (EKG) and arterial pressure (AP) data are shown in sinus rhythm (NSR), atrial asynchronous pacing (AOO), and effective atrial inhibited (AAI) pacing with the device programmed into the DDD mode. There was a need to increase the intrinsic sinus rate for hemodynamic reasons; attempts to overdrive capture the atria were unsuccessful, with atrial pacing spikes occurring throughout the cardiac cycle owing to the premature atrial contractions (middle panel). With atrial sensing in the AAI mode (bottom panel), a modest hemodynamic improvement occurred because of augmentation of the sinus rate but with adequate atrial sensing of the premature contractions.

Postoperative arrhythmias developed in 7 of the 38 patients (Table 6). A junctional tachycardia developed in 1 patient undergoing operation for the Wolff-Parkinson-White syndrome 18 hours postoperatively. The cause of this self-terminating arrhythmia was unclear; it was demonstrated not to be a recurrence of the Wolff-Parkinson-White syndrome, nor was it pacemaker-mediated tachycardia. Three of the remaining 6 patients had a preexisting history of flutter or fibrillation for which they were on preoperative medication. Three of the patients in whom flutter developed had successful entrainment and termination of the flutter using the rapid pacing feature of the 5345 device (see Table 6).

Table 5. Duration of Application of the 5345 Generator[a]

Hours	Applications Terminated (No. of Patients)	Sensing Lost (No. of Patients)
0–24	3	1^A, 1^V
25–48	5	1^A
49–72	1	
73–96	3	
97–120	2	
121–144	6	1^A
145–168	8	
169–192	3	
193–216	. . .	
217–240	1	
241–264	. . .	
265–288	2	
289–312	1	
313–336	1	
337–360	1	1^A (intermittent)
. . .	. . .	
456	1	
. . .	. . .	
667	1	

[a] Mean duration of application, 166 ± 13.7 hours; range, 17 to 667 hours.

^{A} = atrial sensing, ^{V} = ventricular sensing.

There were no episodes of crosstalk or of pacemaker-mediated tachycardia in this study.

Comment

The difference between AV sequential (DVI) pacing and universal DDD pacing results from the presence of an atrial sensing circuit capable of tracking the patient's intrinsic sinus rhythm. This allows for use of a number of pacing modes not available on the DVI devices. The term *universal DDD* means that these additional modes (eg, AAI, VDD) will become effective as the patient's own conduction system interacts with the programmed parameters.

Table 6. Postoperative Atrial Arrhythmias (7 patients, 18.4%)

Operation	Arrhythmia
CABG	Flutter[a]
CABG	Fibrillation
WPW	Junctional tachycardia
AVNR	Flutter[a]
CABG/VT	Flutter
CABG	Fibrillation
CABG/AICD	Flutter[a]

[a] Converted to sinus rhythm by rapid atrial pacing with 5345 device.

AICD = automatic implantable cardioverter-defibrillator; AVNR = cryoablative surgery for atrioventricular nodal reentry; CABG = coronary artery bypass grafting; VT = endocardial resection and cryosurgery for ventricular tachycardia; WPW = ablation of Wolff-Parkinson-White syndrome.

The development of temporary atrial sensing circuitry to permit external DDD pacing has been complicated by several factors. Questions regarding optimal parameters for sensing P waves of 2 to 5 mV amplitude, the duration of atrial sensing capability, the potential for crosstalk between atrial and ventricular circuits, and the potential for pacemaker-mediated tachycardia have at least in part been responsible for the delayed development and application of this technology to external pacing.

Theoretically, patients at the two extremes of the age spectrum in cardiac surgery would benefit most from this technology. As the age of patients undergoing open heart operations has increased, a greater number of patients have been seen for operation with preexisting arrhythmias that require atrial sensing capability for optimal electrophysiologic or hemodynamic performance. The importance of this is magnified in the setting of ventricular dysfunction. At the other extreme, the inability to track a fast sinus rate in the setting of heart block after a congenital heart operation has continued to be a problem.

Considerations that pertain to the electrophysiologic benefits of DDD as compared with DVI pacing in postoperative cardiac patients include (1) the ability to track a variable atrial rate, (2) the ability to pace the atria, ventricle, or both as the circumstances dictate without reprogramming the device, (3) a reduced risk of pacemaker-induced arrhythmias, (4) a decrease in atrial and junctional arrhythmias, and (5) atypical applications in postoperative arrhythmia cases, as demonstrated in the patient with the left atrial isolation procedure in this series. The electrophysiologic benefit of AV sequential pacing as compared with atrial or ventricular pacing has been well demonstrated in the past with the DVI devices.

Considerations that pertain to the hemodynamic benefits of DDD as compared with DVI pacing include (1) the ability to optimize the ventricular response to changes in sinus rate mediated by metabolic demand, and (2) the ability to track the atria with simultaneous ventricular pacing. This circumstance most often occurs in the setting of normal sinus node function but transient AV delay, where overdrive atrial pacing to capture the atrium results in prohibitively fast atrial pacing rates. Until now, the only alternative in that situation was to resort to ventricular pacing, with concomitant loss of atrial synchrony and atrial transport function. As mentioned, in the setting of infants with congenital heart disease or in patients with poor ventricular function who are dependent on atrial transport for optimal hemodynamic performance this can be of extreme importance. Use of this pacing technique has in isolated cases been shown to permit more optimal timing of intraoperative balloon support, thus augmenting hemodynamic performance as well.

Whether provision of atrial sensing capability will in fact have an impact on the occurrence of postoperative supraventricular arrhythmias cannot be determined from this study. The occurrence of PACs is ubiquitous after cardioplegic arrest; however, it has never been demonstrated that a relationship between PACs and postoperative fibrillation or flutter exists. Electrophysiologic theory would dictate that this should be the case, however, and the ability to inhibit pacemaker output after a PAC should theoretically reduce the trigger mechanism for these arrhythmias during the vulnerable postoperative period. These arrhythmias developed postoperatively in only 4 of 37 patients undergoing cardioplegic arrest without an antecedent history of fibrillation or flutter; this incidence is somewhat lower that the incidence of these arrhythmias in other patients undergoing operation at our institution. Nevertheless, further data are necessary to determine if an actual decrease in postoperative arrhythmias can be brought about by use of this device.

The data from this study confirm that interelectrode distance is important for optimal atrial sensing. Theoretically, the optimal interelectrode distance is a function of the conduction velocity in the tissue, whether the bipolar pair is aligned parallel or perpendicular to the long axis of the muscle fibers, and the bandpass filter of the atrial sensing amplifier [15]. Conduction velocity along the long axis of cardiac muscle fibers is greater (approximately 1 m/s) than velocity perpendicular to the long axis (approximately 0.3 to 0.5 m/s); this is referred to as the anisotropic principle of cardiac muscle conduction [16]. The bandpass filter in the Medtronic 5345 external generator for the atrial sensing circuit is 60 to 110 Hz; an interelectrode distance of 0.8 cm places the first cutoff at approximately 110 Hz. Lengthening the distance moves the first cutoff into the filter range and thus signal amplitude is lost, making sensing more difficult. More closely spaced electrodes could theoretically yield better sensing parameters, but this becomes impractical when using individual hook wire electrodes owing to the possibility of one wire shorting out on the other wire.

The anatomical location of the electrode pair on the right atrium also appears to be important for optimal sensing. In the initial description of temporary pacing wires in postoperative patients, Hodam and Starr [17] described placement of the atrial wires positioned "so that the stimulus passes across the region of the S-A node." One wire was passed into the superior vena cava into the right atrial cavity, and the other was placed on the right atrial wall, between the aorta and the superior vena cava or subcutaneously on the chest wall. Waldo and MacLean [8] suggested that the atrial wires should be secured to the epicardium high on the free wall of the right atrium, approximately 0.5 to 1.0 cm apart. Because only the ability to pace was of concern in these situations, optimal conditions for sensing were not considered. Close proximity to the "classical" anatomical S-A nodal tissue was considered adequate.

However, recent experimental and clinical mapping studies by Boineau and associates [18] suggest that in fact an atrial pacemaker complex exists that encompasses a wide range of atrial tissue. This complex has been shown to be present adjacent to the crista terminalis extending between the superior and inferior venae cavae. It is possible that the improved atrial sensing seen with electrode placement on the free wall allows for maximal exposure to the entire complex and not just one end. If in fact the sinus rate is regulated by changing dominance of different pacemaker cells located throughout the complex, then the P wave amplitude will vary according to the dominant cells and sensing will vary accordingly. It follows that attempts to optimize sensing by accurate electrode placement intraoperatively are important to provide adequate sensing in all patients. For theoretical reasons, placing the electrodes along the long axis of the underlying pectinate muscle fibers (which also places the electrodes along the axis of the P wave vector) takes advantage of the increased conduction velocity that occurs along the direction of these fibers.

We would currently recommend, therefore, that atrial electrodes be placed approximately 0.8 to 1 cm apart on the body of the right atrial free wall (see Fig 4). The bipole of the electrode pair should be oriented along the long axis of the underlying pectinate muscle fibers. This position gives what appear to be reliable thresholds for long-term sensing of P waves while still permitting adequate pacing of atrial tissue.

There were no episodes of crosstalk between the atrial and ventricular circuits and no occurrences of pacemaker-mediated tachycardia in this study. In addition, there were no episodes of myopotential sensing or inhibition of pacemaker output. However, crosstalk and pacemaker-mediated tachycardia remain as theoretical problems with external DDD pacing and must be kept in mind when using this device.

The availability of external DDD pacing will make an important difference in the postoperative management of select patients after open heart operations. An electrophysiologic as well as hemodynamic benefit results from proper use of this form of pacing in a large percentage of patients based on our experience thus far. Additional studies are underway to more carefully localize the optimal site(s) of electrode placement as well as to determine the optimal filtering parameters for the atrial sensing circuitry.

References

1. Harris PD, Singer DH, Malm JR, Hoffman BF. Chronically implanted cardiac electrodes for diagnostic, therapeutic and investigational use in man. J Thorac Cardiovasc Surg 1967; 54:191–8.
2. Waldo AL, MacLean WAH, Karp RB, Kouchoukos NT, James TN. Continuous rapid atrial pacing to control recurrent or sustained supraventricular tachycardias following open heart surgery. Circulation 1976;54:245–50.
3. Waldo AH, MacLean WAH, Karp RB, Kouchoukos NT, James TN. Entrainment and interruption of atrial flutter with atrial pacing. Circulation 1977;56:737–45.
4. Waldo AH, MacLean WAH, Cooper TB, Kouchoukos NT, Karp RB. Use of temporarily placed epicardial atrial wire electrodes for the diagnosis and treatment of cardiac arrhythmias following open-heart surgery. J Thorac Cardiovasc Surg 1978;76:500–5.
5. Chamberlain DA, Leinbach RC, Vassaux CE, Kastor JA, DeSanctis RW, Sanders CA. Sequential atrioventricular pacing in heart block complicating acute myocardial infarction. N Engl J Med 1970;282:577–82.

6. Fields J, Berkovits BV, Matloff JM. Surgical experience with temporary and permanent AV sequential demand pacing. J Thorac Cardiovasc Surg 1973;66:865–77.
7. Hartzler GO, Maloney JD, Curtis JJ, Barnhorst DA. Hemodynamic benefits of atrioventricular sequential pacing after cardiac surgery. Am J Cardiol 1977;40:232–6.
8. Waldo AH, MacLean WAH. Diagnosis and treatment of cardiac arrhythmias following open heart surgery. Mt. Kisco, NY: Futura, 1980.
9. Wish M, Fletcher RD, Cohen A. Hemodynamics of AV synchrony and rate. J Electrophysiol 1989;3:170–5.
10. Littleford PO, Schwartz KM, Pepine CJ. A temporary external DDD pacing unit. Am J Cardiol 1984;53:1041–3.
11. Billhardt RA. Temporary pacing. Clin Prog Pacing Electrophysiol 1984;2:305–24.
12. Haffajee CI. Temporary cardiac pacing: modes, evaluation of function, equipment, and trouble shooting. Cardiol Clin 1985;3:515–26.
13. Hauser RG, Vicari RM. Temporary pacing: indications, modes and techniques. Med Clin N Am 1986;70:813–26.
14. Wallenhaupt SL, Rogers AT. Intraoperative use of dual-chamber demand pacemakers for open heart operations. Ann Thorac Surg 1989;48:579–81.
15. Basmajian JV, De Luca CJ. Apparatus, detection and recording techniques. In: Basmajian JV, De Luca CJ, eds. Muscles alive: their functions revealed by electromyography. 5th ed. Baltimore: Williams and Wilkins, 1985:19–64.
16. Spach MS, Dobler PC, Heidlage JF. Resolution of discontinuous versus continuous propagation: microscopic mapping of the derivatives of extracellular potential waveforms. In: Zipes DP, Jalife J, eds. Cardiac electrophysiology: from cell to bedside. Philadelphia: W.B. Saunders, 1990:139–49.
17. Hodam RP, Starr A. Temporary postoperative epicardial pacing electrodes. Ann Thorac Surg 1969;8:506–10.
18. Boineau JP, Canavan TE, Schuessler RB, Cain ME, Corr PB, Cox JL. Demonstration of a widely distributed atrial pacemaker complex in the human heart. Circulation 1988;77:1221–37.

DISCUSSION

DR LENOX D. BAKER, JR (Norfolk, VA): I would like to thank you for an excellent presentation of something that has been too long in coming. I think that the pacing industry, although it has developed a lot of superb permanent products, has been slow in responding to our need for this type of temporary device.

We are seeing an increasing number of patients with poor left ventricular function who come to operation not on β-blockers and therefore come off bypass after extensive revascularization with complete atrioventricular block and fast atrial responses. Some of these patients require intraaortic balloon pumping to come off bypass, and over the last 5 years we have had several dozen patients in whom we have used a device similar to this. We have been able to then track the atrial rate and have an appropriate timed ventricular pace rather than have them in varying rhythms in which we have been unable to synchronize a balloon pump. The establishment of the DDD pacing in these patients has allowed us to get them off bypass when before that we could not. I am curious if you have had any experience with the coordination of this unit with an intraaortic balloon pump.

We have also been testing a device similar to this one but from another company and have had several instances of pacemaker crosstalk. They have eventually been able to work these problems out, but I am curious to know whether you have seen any problems with pacemaker crosstalk in your current series. By crosstalk I am referring to the suppression of the ventricular output by the atrial output.

DR FERGUSON: In answer to your first question, in this series of patients, none required intraaortic balloon pumping. We have subsequently had experience in a number of patients with exactly that circumstance. There are 2 who I can recall in whom we had great difficulty getting them off bypass with an intraaortic balloon pump, not so much for hemodynamic reasons but because of inability to track the patient's supraventricular tachycardias.

With regard to your second question, the two main problems with applying external DDD pacing based on the experience with permanent DDD pacemakers were thought to be problems with crosstalk between the atrial and the ventricular sensing channels, and also the induction of pacemaker-mediated tachycardia. In our experience we have not had any problems with crosstalk using the device that we have evaluated, nor have we had any incidence of pacemaker-mediated tachycardia. This circumstance occurs when a patient who has the capability of ventriculoatrial conduction has a premature ventricular contraction, which then sets up the reentrance circuit with the pacemaker as part of that circuit. In the total clinical experience in the evaluation of this device in more than 250 patients, there was only one documented episode of pacemaker-mediated tachycardia, so that is probably going to be less of a problem than was anticipated.

DR JOHN M. KRATZ (Charleston, SC): Those of us who have been involved in this type of pacing have all recognized fairly early, I think, that the main problem is atrial sensing, and we all owe Dr Ferguson and Dr Cox our thanks for showing us how to get better P waves on these atrial wires. I think that is going to be a great amount of help.

I would like to point out a little paradox. Most of us will have to decide in the next year or two whether we will want to be using these more complex DDD devices or our more familiar DVI devices; we have seen today some examples of how the DDD device helps hemodynamically. There is no doubt about that. But for the routine, day-to-day patient who is being paced after coronary bypass grafting or some other type of heart operation, DVI pacing works rather well. As long as one is a bit observant of what the atrial rate is and adjusts the DVI pacemaker appropriately, the hemodynamic results are the same in most cases.

The other side of the story is that these devices are fairly complex, and when we start having our junior house officers and our nursing staff make adjustments to these fairly complex DDD devices, there is a real potential for rather bizarre pacing and some rather interesting effects. We are all going to have to go back to school and pay a bit more attention to our postoperative pacing when we use these devices.

DR FERGUSON: I would agree with those comments.

Comparison of Postoperative Complications Between Saphenous Vein and IMA Grafts to Left Anterior Descending Coronary Artery

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Considerable controversy exists regarding relative morbidity associated with the saphenous vein graft (SVG) and internal mammary artery (IMA) graft in patients undergoing myocardial revascularization. As a part of the cooperative study on use of antiplatelet drugs for graft patency, operative and postoperative data were prospectively collected on 1,150 patients who underwent either SVG (n = 656) or IMA anastomosis (n = 494) to the left anterior descending coronary artery. There were no differences in baseline characteristics of patients, distribution of randomization among treatment groups, and total number of distal anastomoses performed between the two groups. The aortic cross-clamp time, cardiopulmonary bypass duration, operative time, and chest tube drainage were greater ($p = 0.0001$) in the patients with IMA grafts compared with SVG. However, there was no difference in the operative mortality rate, the amount of blood and blood products received, the reoperation rate for control of postoperative bleeding, and incidence of wound complications between the two groups. The early and 1-year patency rates for the IMA were slightly but not significantly better than the SVG patency rates (92.8% versus 90.1% for 1-year patency; $p = 0.309$). In conclusion, use of IMA is associated with a longer operative time as well as increased postoperative bleeding compared with the SVG. It, however, does not increase operative mortality or postoperative morbidity.

(Ann Thorac Surg 1991;51:733–8)

During the past few years enthusiasm to use the internal mammary artery (IMA) has markedly increased, and the IMA currently is considered by many to be the conduit of choice as a bypass graft. This is based on the recent reports that have demonstrated that the late IMA patency rates are superior to that of saphenous vein grafts (SVGs). Patients receiving IMA grafts also tend to have improved long-term survival and a reduction in the rate of repeat revascularization procedures, as well as in late cardiac events [1–3]. This conclusion, however, has not been scrutinized by controlled, prospective, randomized trials.

The relative complication rates associated with use of the SVG versus the use of the IMA alone or in combination with saphenous vein grafting remains controversial. The majority of the reported studies have focused on the incidences of wound complications [4, 5]. The purpose of this communication is to compare the operative mortality rates, the amount of blood and blood products administered, and incidences of postoperative complications in patients who have received either a vein graft or IMA graft to the left anterior descending coronary artery (LAD).

Material and Methods

The data analyzed for this report were derived from two Department of Veterans Affairs Cooperative Studies entitled "Antiplatelet therapy after coronary artery bypass graft surgery I and II." The purpose of these prospective, centrally directed, randomized, double-blind, placebo-controlled multicenter trials was to evaluate the effect of antiplatelet therapy on the patency of coronary artery bypass grafts. Although the primary goal of these studies was to examine the patency of vein grafts, IMA graft patency was also assessed because many individuals received IMA grafts in addition to saphenous veins. There was no randomization, however, to IMA versus vein graft to the LAD.

The research protocols and consent forms were reviewed and approved by the Human Rights Committee of the Department of Veterans Affairs Cooperative Studies Program Coordinating Center, Hines, IL, as well as the Human Subjects Committee at each of the participating centers. Each participant gave written informed consent before entering the study.

Detailed information from the preoperative patient history, physical examination, laboratory tests, electrocardiogram, and coronary angiogram, as well as detailed perioperative data, were collected prospectively in a standardized manner. Definition of the study population, treatment regimens, the exclusion criteria, and stratification methods have been previously described [6, 7].

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Study Population

Between June 1983 and 1988, 6,159 patients underwent coronary artery bypass grafting (CABG) at 14 participating Department of Veterans Affairs Medical Centers (see Appendix 1 for complete listing of principal investigators and participating centers). Of the number of patients undergoing CABG in these institutions, 1,261 patients were enrolled in one of the two protocols. The most common reasons for excluding patients were emergency operations and scheduling difficulties that precluded the administration of preoperative study medications, patient refusal to participate, previous CABG, necessity of concomitant valve replacement, and other diseases that required the long-term use of aspirin or prostaglandin inhibiting agents. All patients who received either a vein graft or an IMA graft to the LAD were considered for analyses for this report. However, patients who received bilateral IMAs, or a right IMA to the LAD, or both an IMA and an SVG to the LAD were excluded from the analyses. Thus, the study population for this communication consisted of 1,150 patients.

Surgical Procedures

The operative procedure was performed by the standard protocol at each participating center by either the attending cardiac surgeon or a surgical resident under the supervision of the attending surgeon. The decision to use the IMA or saphenous vein as a conduit was made by the surgical team. Details of the operation, including mode of myocardial preservation, anastomotic technique, suture material, postoperative care, and indications for reoperation to control postoperative bleeding were accomplished at the discretion of the operating surgeons. These details, as well as aortic cross-clamp time, duration of cardiopulmonary bypass, total operative time, chest tube drainage, volume of blood and blood products administered, and perioperative complications were recorded on a standardized surgical data form.

Statistical Analysis

Comparability of patients having saphenous vein versus IMA grafts was tested using the χ^2 statistic on qualitative variables. Quantitative variables were evaluated one of two ways. Student's *t* test was used to analyze normally distributed data. The mean ± standard deviation is presented for these data. The Wilcoxon rank-sum test was used to analyze non–normally distributed data. The mean ± standard deviation is presented, as well as median value (50th percentile) as the measure of central tendency. All analyses for IMA and SVGs were performed irrespective of treatment group.

Results

Of 1,150 patients analyzed in this report, 656 patients underwent saphenous vein grafting to the LAD and 494 patients had an IMA graft to the LAD. The baseline patient characteristics are shown in Table 1. Although there is a statistically significant difference in the mean ages, the difference is not clinically important (59.7 ± 7.6 versus 58.8 ± 7.6 years). A higher proportion of patients in the SVG group received aspirin therapy preoperatively (58.4% versus 53%; $p = 0.070$), and they also had higher levels of high-density lipoproteins. There were no significant differences in any of the other baseline variables between the two groups.

Table 1. Comparison of Baseline Variables Between Patients Receiving an SVG and IMA Graft to the LAD

Variable	SVG (n = 656)	IMA (n = 494)	*p* Value
Age (y)	59.7 ± 7.6	58.8 ± 7.6	0.041
Extent of CAD (%)			0.157
One vessel	3.5	2.2	
Two vessel	17.8	21.5	
Three vessel	78.7	76.3	
Left main CAD (%)	16.3	15.0	0.543
Patients on aspirin (%)	58.4	53.0	0.070
Angina (%)	97.3	97.4	0.905
Hypertension (%)	47.8	50.3	0.397
Prior MI (%)	58.0	58.4	0.874
Diabetes mellitus (%)	9.0	8.5	0.766
Cigarette smoking (pack years)			
Past	40	40	0.642
Current	49	45	0.718
Functional class (I–IV)	3.2 ± 0.8	3.3 ± 0.9	0.073
Serum cholesterol (mmol/L)	5.74 ± 1.22	5.74 ± 1.34	0.881
Serum triglycerides (mmol/L)	2.12	1.98	0.148
Serum HDL (mmol/L)	0.91	0.83	0.001
Size of distal LAD (mm)	1.7 ± 0.5	1.8 ± 0.4	0.144
Avg No. of distal anastomoses	3.5 ± 1.0	3.4 ± 0.9	0.076

CAD = coronary artery disease; HDL = high-density lipoprotein; IMA = internal mammary artery; LAD = left anterior descending coronary artery; MI = myocardial infarction; SVG = saphenous vein graft.

The aortic cross-clamp time, duration of cardiopulmonary bypass, and total operative time were significantly longer in the patients with IMA grafts compared with those receiving vein grafts (Table 2).

The blood loss through the chest tubes in the IMA group was 1,457 ± 963 mL (range, 100 to 7,685 mL; median, 1,174 mL) compared with 1,053 ± 781 mL (range, 10 to 8,140 mL; median, 827 mL) in the SVG group ($p = 0.0001$). The mean ± standard deviation and median volume of red blood cells and other blood products

Table 2. Operative Durations

Duration	SVG (n = 656)	IMA (n = 494)	*p* Value
Aortic cross-clamp time (min)	52 ± 22	60 ± 23	0.0001
CPB duration (min)	100 ± 40	110 ± 38	0.0001
Total operative time (min)	237 ± 87	275 ± 80	0.0001

CPB = cardiopulmonary bypass; IMA = internal mammary artery; SVG = saphenous vein graft.

Table 3. Volume of Blood and Blood Products Administered (all patients)

	SVG[a]			IMA[a]			
Product	% Patients Receiving Product	Mean ± SD (units)	Median (units)	% Patients Receiving Product	Mean ± SD (units)	Median (units)	*p* Value
RBC	86	4.1 ± 3.9	3.6	85	4.3 ± 4.0	3.6	0.877
FFP	60	2.8 ± 3.6	1.8	56	2.6 ± 3.5	1.6	0.147
Platelets	32	3.9 ± 7.5	0	37	4.4 ± 8.1	0	0.140
Cryoprecipitate	4	0.5 ± 4.1	0	5	0.7 ± 3.6	0	0.421

[a] 58.4% of patients in the SVG group and 53.0% in the IMA group received aspirin preoperatively.

IMA = internal mammary artery; FFP = fresh frozen plasma; RBC = red blood cells; SD = standard deviation; SVG = saphenous vein graft.

administered are shown in Table 3. These values are based on all 1,150 patients irrespective of whether they received the blood products or not. Table 4 shows the values of blood products in the group of patients who received them. There was no difference in the volume of blood or blood products administered between the two groups. Seven percent of the patients in the SVG group and 10% in the IMA group did not receive any blood or blood products ($p = 0.095$).

The incidences of various postoperative complications are listed in Table 5. The operative mortality was slightly but not significantly higher in patients receiving an SVG (3.2% versus 2.2%; $p = 0.320$). Although the postoperative blood loss was greater in the IMA group, there was no difference between the two groups for the number of patients who required reoperation for control of postoperative bleeding (5.2% for SVG versus 4.3% for IMA). The patients with IMA grafts had a modest but nonsignificant increased incidence of postoperative pulmonary complications (5.5% versus 3.7%, $p = 0.141$). The incidence of median sternotomy wound complications (superficial as well as deep) was 2.2% in the IMA group and 2.0% in the SVG group, and the occurrence of deep mediastinitis was identical in both groups (0.8%).

Comment

There is a growing enthusiasm for using the IMA for myocardial revascularization because patients receiving IMA grafts to the LAD appear to have increased longevity and greater freedom from cardiac events than the patients receiving only SVGs. Recently, antiplatelet drugs have been shown to improve the patency rates of SVGs to the point that these 1-year patency rates are comparable with those achieved for IMA grafts [7].

We have also been interested in evaluating whether any differences exist between patients receiving the IMA graft versus the SVG to the LAD with respect to postoperative complications and the requirements of blood and blood products. Most reports on the complications associated with IMA grafting have been limited to sternotomy wound problems. The current study shows that the aortic cross-clamp time, cardiopulmonary bypass duration, total operative time, and the postoperative blood loss were all greater in patients receiving IMA grafts as opposed to saphenous vein grafts. However, there were no differences between the two groups with respect to operative mortality, requirements for blood and blood products, the reoperation rate for control of bleeding, and the incidence

Table 4. Volume of Blood and Blood Products Administered (for patients receiving the product)

	SVG		IMA		
Product	Mean ± SD	Median	Mean ± SD	Median	*p* Value
RBC (units)	4.8 ± 3.8	4.0	5.1 ± 3.8	4.0	0.530
FFP (units)	4.7 ± 3.5	4.0	4.6 ± 3.6	3.6	0.496
Platelets (units)	11.9 ± 8.8	10.0	11.8 ± 9.6	10	0.755
Cryoprecipitate (units)	11.5 ± 17.0	9	13.1 ± 9.9	10	0.065

IMA = internal mammary artery graft; FFP = fresh frozen plasma; RBC = red blood cells; SD = standard deviation; SVG = saphenous vein graft.

Table 5. Postoperative Complications[a]

Complication	SVG	IMA	*p* Value
Death	3.2	2.2	0.320
Atrial arrhythmias	21.2	24.3	0.206
Ventricular arrhythmias	17.8	18.7	0.719
Ventricular arrhythmias with cardiac arrest	3.7	2.2	0.164
Myocardial infarction	6.3	4.5	0.190
Low cardiac output	5.8	5.9	0.949
Hemorrhage requiring reoperation	5.2	4.3	0.473
Pneumonia	2.7	4.5	0.116
Respiratory failure	1.2	1.8	0.402
Pulmonary embolus	0.8	0.6	0.754
Superficial wound infection	1.2	1.6	0.564
Mediastinitis	0.8	0.8	0.925
Renal failure	0.6	1.0	0.441

[a] All values are shown as percentages.

IMA = internal mammary artery; SVG = saphenous vein graft.

of other postoperative complications including sternal wound infections.

The development of sternal wound complications is one of the major theoretical disadvantages of using the IMA. Culliford and associates [8] reported a 1.1% incidence of mediastinitis in patients who had only saphenous grafts. This incidence doubled in patients receiving a single IMA implantation and increased eightfold (8.5%) when bilateral IMAs were used. Sternal ischemia and a greater incidence of postoperative bleeding requiring reoperation were cited as predisposing risk factors. Grossi and associates [9] reported an overall infection rate of 1.6% among 2,300 patients undergoing isolated myocardial revascularization procedures. However, for patients who had at least one IMA graft, the incidence of mediastinitis was 2.2% compared with 0.8% when no IMA was used. The course of infection also appeared to be more severe in the IMA patients, with the hospitalization being significantly longer. In this study, however, we did not observe any difference in the incidence of wound complications between IMA and SVG patients. Similarly, other investigators also disagree with the assessment that wound complications are associated with the use of single or bilateral IMAs. Nevertheless, for some cohorts of patients (elderly, female, obese, diabetic) use of the IMA may pose an increased risk of postoperative morbidity [10–12].

Though there was a statistically significant increase in the postoperative blood loss in the patients receiving IMA grafts, it was probably not clinically significant as the patients in the IMA group neither received more blood products nor had a greater incidence of reoperation for control of postoperative bleeding than the patients receiving the SVG. The amount of blood administered to our patients was greater than that reported by the Cleveland Clinic [10]; however, more than half of the patients in this study were on aspirin therapy preoperatively. Preoperative administration of aspirin in patients undergoing CABG is associated with increased postoperative blood loss, as well as increased requirement of blood transfusion [13, 14]. During the course of this study we observed a decrease in the administration of blood during the later part of the study; however, there was no change in the overall postoperative blood loss. Between 1983 and 1986, the patients with IMA grafts and SVGs received 5.0 ± 3.8 units and 4.5 ± 4.0 units of red blood cells, respectively, and for the period between 1986 and 1988 these requirements decreased to 3.9 ± 4.0 and 3.4 ± 2.8 units, respectively. The decision for blood transfusion and reinfusion of shed mediastinal blood, as well as the acceptable level of hematocrit at discharge, were left to the discretion of the individual investigator. Cosgrove and colleagues [10] reported a higher transfusion requirement for the patients receiving vein grafts compared with patients receiving IMA grafts. They also demonstrated that preoperative red cell mass and age were the two best predictors of the necessity for and amount of blood transfusion in patients undergoing myocardial revascularization. However, Ferraris and Gildengorin [15] did not identify blood cell volume as an independent predictor of postoperative blood requirement. Taggart and associates [14] reported the use of preoperative aspirin as the most important independent predictor for blood loss as well as blood requirement.

It is not surprising that patients receiving IMA grafts had a longer aortic cross-clamp time, cardiopulmonary bypass duration, and total operative time. It requires extensive dissection to take down the IMA pedicle from the chest wall, and the anastomosis of IMA to LAD is also technically more difficult and demanding than the anastomosis of SVG to the LAD. However, these risk factors did not result in increased postoperative morbidity in the IMA group.

There was a modest but nonsignificant increase in the pulmonary complications (pneumonia and respiratory failure) observed in the IMA patients (5.5% versus 3.7%; $p = 0.141$). This could be due to many factors including opening of the pleural sac and placement of the chest tubes, possible injury to the phrenic nerve, trauma to the chest wall while harvesting the IMA pedicle, and the development of postoperative pleural effusion. In our experience, as well as that of others, IMA patients tend to have more left anterior chest wall discomfort, especially in the costochondral area, than patients with SVGs. This is probably due to sternal retraction required for dissection of the IMA pedicle at the time of operation [16, 17]. This may result in splinting of the chest wall leading to hypoventilation, inadequate cough, retention of secretions, and atelectasis. Combination of these factors may predispose the patients to pulmonary infection and respiratory failure.

There was no difference in the early (7 to 10 days) or 1-year graft patency rates between the two groups. The early graft patency rates were 96.7% for SVGs and 96.4% for the IMA grafts ($p = 0.792$). The 1-year graft patency rates were 90.1% and 92.8%, respectively ($p = 0.309$) [7]. However, we do not have the late patency data (5 to 10 years and beyond) in this cohort of patients. The superior late patency of the IMA has been cited as one of the main reasons for using the IMA as the bypass conduit of choice. The data from the Montreal Heart Institute suggest an approximately 53% patency rate of the SVG at 10 years, whereas approximately 90% patency rate has been reported for the IMA grafts [18–20]. However, these data were not prospectively acquired and the patients undergoing late IMA angiography represent only a small fraction of the original cohorts who have undergone CABG.

In conclusion, this retrospective, nonrandomized study revealed no significant difference in operative mortality or postoperative morbidity when the IMA or the SVG is used to bypass the LAD. This suggests that the decision to use the IMA or SVG should not be based on the potential operative or postoperative complications.

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References

1. Spencer FC. The internal mammary artery: the ideal coronary bypass graft. N Engl J Med 1986;314:50–1.
2. Gardner TJ, Greene PS, Rykiel MF, et al. Routine use of the left internal mammary artery graft in the elderly. Ann Thorac Surg 1990;49:188–94.
3. Johnson WD, Brenowitz JB, Kayser KL. Factors influencing long term (10 year to 15 year) survival after a successful coronary artery bypass operation. Ann Thorac Surg 1989;48:19–25.
4. Loop FD, Lytle BW, Cosgrove DM, et al. Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. Ann Thorac Surg 1990;49:179–87.
5. Cosgrove DM, Lytle BW, Loop FD, et al. Does bilateral internal mammary artery grafting increase surgical risk? J Thorac Cardiovasc Surg 1988;95:850–6.
6. Goldman S, Copeland J, Moritz T, et al. Improvement in early saphenous vein graft patency after coronary artery bypass surgery with antiplatelet therapy: results of a Veterans Administration Cooperative Study. Circulation 1988;77:1324–32.
7. Goldman S, Copeland J, Moritz T, et al. Internal mammary artery and saphenous vein graft patency: effects of aspirin. Circulation 1990;82(Suppl 4):237–42.
8. Culliford AT, Cunningham JN, Zeff RH, et al. Sternal and costochondral infections following open heart surgery: a review of 2594 cases. J Thorac Cardiovasc Surg 1976;72:714–26.
9. Grossi EA. Discussion of Loop FW, Lytle BW, Cosgrove D, et al. Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. Ann Thorac Surg 1990;49:187.
10. Cosgrove DM, Loop FD, Lytle BW. Does mammary artery grafting increase surgical risk? Circulation 1985;72(Suppl 2):170–4.
11. Wilson APR, Livesey SA, Treasure T, et al. Factors predisposing to wound infection in cardiac surgery, a prospective study of 517 patients. Eur J Cardiothorac Surg 1987;1:158–64.
12. Acinapura AJ, Rose DM, Jacobowitz IJ, et al. Internal mammary artery bypass grafting: influence on recurrent angina and survival in 2,100 patients. Ann Thorac Surg 1989;48:186–91.
13. Sethi GK, Copeland JG, Goldman S, et al. Implications of preoperative administration of aspirin in patients undergoing coronary artery bypass grafting. J Am Coll Cardiol 1990;15:15–20.
14. Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. Ann Thorac Surg 1990;50:425–8.
15. Ferraris VA, Gildengorin V. Predictors of excessive blood use after coronary artery bypass grafting. A multivariate analysis. J Thorac Cardiovasc Surg 1989;98:492–7.
16. Mailis A, Chan J, Basinski A, et al. Chest wall pain after aortocoronary bypass surgery using internal mammary artery graft: a new pain syndrome? Heart Lung 1989;18:553–8.
17. Jansen KJ, McFadden PM. Postoperative nursing management in patients undergoing myocardial revascularization with the internal mammary artery bypass. Heart Lung 1986;15:48–54.
18. Grondin CM, Campeau L, Lespérance J, Enjalbert M, Bourassa MG. Comparison of late changes in internal mammary artery and saphenous vein grafts in two consecutive series of patients 10 years after operation. Circulation 1984;70(Suppl 1):208–12.
19. Fiore AC, Naunheim KS, Dean P, et al. Results of internal thoracic artery grafting over 15 years: single versus double grafts. Ann Thorac Surg 1990;49:202–9.
20. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10 year survival and other cardiac events. N Engl J Med 1986;314:1–6.

Appendix 1

Chairman's Office

Steven Goldman, MD, and Jack G. Copeland, MD (Study Co-Chairmen), Karen Zadina, RN, MA (Study Coordinator), Katherine Handley, Patricia Pettijohn* (Secretaries).

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Cooperative Studies Program Central Administration (Department of Veterans Affairs Central Office, Washington, DC)

Daniel Deykin, MD (Chief), Ping C. Huang, PhD (staff assistant), Janet Gold (administrative officer).

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* Former participant.

DISCUSSION

DR HENDRICK B. BARNER (St. Louis, MO): The divisions of cardiology and cardiothoracic surgery at St. Louis University have randomized 325 patients into a study of antiplatelet therapy and placebo control. Patients received dipyridamole, 100 mg four times daily, for 2 days, 100 mg preoperatively, and 100 mg 90 minutes postoperatively, and were then given dipyridamole, 75 mg three times daily, and aspirin, 325 mg three times daily.

Cardiac catheterization at 1 month and 1 year revealed a 1-year patency for vein grafts of 92% in the treated group versus 85% ($p < 0.01$) in controls. For IMA grafts the patency was 98% and 95%, these differences not being significant. Patency for IMA grafts was better than vein graft patency with or without therapy. Despite the apparent success of this antiplatelet regimen, we have reverted to our previous treatment of 325 mg of aspirin a day as antiplatelet therapy.

There was no difference in measured postoperative blood loss or in transfusion requirements when the placebo patients were compared with treated patients.

DR SETHI: We have previously presented the data from this cooperative study, which show that preoperative administration of aspirin improves the early as well as late (1-year) patency of the vein grafts. We also showed that addition of dipyridamole to aspirin does not further improve graft patency over the aspirin alone. However, preoperative administration of aspirin does increase postoperative blood loss. This has been subsequently confirmed by other reports as well.

DR JOHN M. KRATZ (Charleston, SC): I must take issue with your final conclusion.

As you pointed out, your patients were not randomized, and therefore I think most of us have to believe that the surgeons doing these procedures made some judgment about potential complications and problems in their decision to use a vein graft or an IMA. Then to say that the use of an IMA or vein graft does not influence the postoperative results just does not make sense. Your surgeons may well have selected for potential problems when they decided to use a vein graft.

DR SETHI: I agree with you, and you are absolutely right that these patients were not randomized between IMA and SVGs. This is one of the drawbacks of this study. The ideal study would have been to randomize patients between IMA and the SVG. As you yourself know, it is very difficult to conduct this type of study at present, especially knowing the data that exist in the literature.

We have compared the basline characteristics of the two groups and they appear to be comparable, which makes me believe that the data and conclusions are valid. We did approach participants for the possibility of a subsequent study randomizing patients between IMA and the vein graft, and as you would expect not many surgeons and especially not many cardiologists were eager to participate in such a study.

Pretreatment With Nicardipine Preserves Ventricular Function After Hypothermic Ischemic Arrest

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Calcium antagonists have a protective effect on postischemic myocardial function when included in normothermic cardioplegia solutions. This effect varies with the calcium antagonist, but is generally lost under hypothermic conditions. The hypothesis tested was that a calcium antagonist would increase postischemic myocardial performance if given before the onset of hypothermic arrest. Isolated working rat hearts were used with an oxygenated modified Krebs-Henseleit buffer solution as a perfusion media. Rats were pretreated with 1 of 9 doses of a nicardipine solution (0 to 100 μg/kg, intraperitoneally) 20 minutes before excision of the heart. Nicardipine is a light-stable, water-soluble calcium antagonist with minimal myocardial depressant effects. The hearts were arrested for 25 minutes at 37°C or 93 minutes at 24°C with 20 mL of cardioplegia solution containing 0.05 mmol/L $CaCl_2$. Postischemic performance and adenosine triphosphate content were used as determinants of efficacy. Eighty-three percent of 101 treated hearts recovered in contrast to a mortality of 50% in the 24 nontreated hearts. Pretreatment with 25 μg/kg significantly increased ($p < 0.05$) the percent recovery (compared with the nontreated group) of the following variables of cardiac function: systolic pressure, 74% to 96% (37°C), 76% to 90% (24°C); cardiac output, 61% to 90% (37°C), 62% to 84% (24°C); stroke work, 49% to 95% (37°C), 50% to 92% (24°C); and adenosine triphosphate, 76% to 87% (37°C), 58% to 68% (24°C). Progressive increases in postischemic function at 37° and 24°C were seen as the dose of nicardipine was increased from 0 to 25 μg/kg and decreased function was seen with a pretreatment dose greater than 25 μg/kg of nicardipine. Pretreatment with nicardipine significantly improved postischemic myocardial performance under hypothermic conditions and should be administered or at least not discontinued before cardiac operations.

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During the last decade increasing interest has developed in the use of calcium antagonists as an adjunct to cardioplegic solutions in an attempt to decrease postischemic myocardial dysfunction secondary to reperfusion injury. Cardioplegia solutions containing a high level of calcium [1] and calcium reentry into the cell upon reperfusion [2–6] have depressive effects on myocardial function. The use of calcium antagonists such as nifedipine, verapamil, or diltiazem has been shown to have a significant protective effect on the myocardium when administered just before or during cardioplegia infusion in isolated rat and rabbit hearts [6–10]. Improvements in overall hemodynamic function or reduction of cardiac enzyme release have also been shown clinically with the use of calcium antagonists during the period of aortic cross-clamping [11–13]. The use of calcium antagonists is, however, still controversial as the protective effect of calcium antagonists has been shown to be variable.

Diltiazem-containing hypothermic crystalloid cardioplegia has a protective effect on the postischemic myocardium [14, 15]. Cold blood diltiazem cardioplegia also provided increased protection in a canine model and in patients [16, 17]. These studies were performed in intact animals and therefore diltiazem had peripheral effects in addition to the myocardial effects. Nifedipine- and verapamil-containing cardioplegic solutions have generally been shown to not have a beneficial effect at temperatures less than 28°C in isolated heart models [5, 6, 10]. This finding has also been reconfirmed in this laboratory with nicardipine-containing cardioplegia. There was significant improvement of postischemic function at 37°C, which was lost at temperatures less than 32°C.

Nicardipine is a 1,4-dihydropyridine derivative that is a light-stable, water-soluble calcium antagonist with minimal myocardial depressive effects. The hypothesis of this experiment was that pretreatment with a calcium antagonist before institution of hypothermic ischemic cardioplegic arrest would increase postischemic performance. This would be achieved by allowing time for incorporation or binding of the calcium antagonist to the myocyte before possible membrane conformation changes induced by hypothermia, which may prevent the action of nicardipine.

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Material and Methods

Experimental Model

The preparation used was an isolated, ex vivo, perfused, working left heart. Hearts were obtained from male Sprague-Dawley rats weighing 300 to 450 g. Each animal was injected intraperitoneally with 1 of 9 doses of a nicardipine solution containing 0 to 100 μg/kg (Cyntex Corp, Palo Alto, CA). The concentrations of the solutions were adjusted so that each animal received between 1 and 1.5 mL of solution. A minimum of 6 rat hearts composed each group. After 15 minutes each animal was injected with 1,000 U of heparin (intraperitoneally) and then anesthetized with 4 mL of a 7.2% solution of chloral hydrate (intraperitoneally), (Fisher Scientific, Fairlawn, NJ). The heart was rapidly excised 5 minutes later and placed in a modified Krebs-Henseleit bicarbonate buffer solution at 2°C (Table 1) and prepared according to a modified Langendorff technique [18].

The aorta was cannulated, and the heart was mounted on a Langendorff apparatus. Retrograde perfusion was started with modified Krebs-Henseleit bicarbonate buffer solution at 37°C. Buffer flowed freely into the aortic root at a pressure of 80 cm H_2O for 15 minutes to allow for recovery and development of a steady nonworking state. Conversion to a working preparation was achieved by placing a second perfusion cannula into the left atrium and infusing buffer solution at a pressure of 20 cm H_2O. The left ventricle ejected against a pressure of 80 cm H_2O into a compliance chamber with a 2.5-mL air cap. The pulmonary artery was widely opened to allow for drainage and collection of coronary sinus effluent. Three temperature circuits permitted buffer, cardioplegia, and each heart to be maintained at any desired temperature. All fluid entering the heart was filtered through 0.2-μm filters (Pall Biomedical Inc, Fajardo, PR). A thermistor (Electromedics, Inc, Englewood, CA) was placed on the left ventricle and the myocardial temperature was kept within 0.5°C of the desired temperature. All buffer solutions were prepared by the National Institutes of Health Media Service on a weekly basis and once added to the apparatus gassed continuously with a mixture of 95% oxygen and 5% carbon dioxide. This resulted in a solution with an osmolarity of 379 mOsm/L, pH of 7.40 to 7.50, carbon dioxide tension of 35 to 45 mm Hg, and oxygen tension greater than 750 mm Hg (Radiometer ABL3, Copenhagen, Denmark). The individual cardioplegia solutions were prepared daily (see Table 1).

Preischemic measurements were made after 15 minutes of perfusion in the working mode. Aortic and coronary flow were measured by timed collection into graduated cylinders. Pressure data were obtained from pressure transducers (Gould P23, Gould Inc, Oxnard, CA) placed in the aortic outflow chamber. Systolic, diastolic, and mean pressure were recorded on an electrostatic recorder (Gould ES2000, Gould Inc). Heart rate was obtained from the pressure tracing. A heart was rejected if the heart rate was less than 200 beats/min, cardiac output was less than 40 mL/min, or the coronary to aortic flow ratio was greater than 0.60, indicating serious iatrogenic injury during preparation.

Table 1. Composition of Modified Krebs-Henseleit Bicarbonate Buffer and Cardioplegia Solutions

Component	Amount
Krebs-Henseleit bicarbonate buffer solution	
KCl (mmol/L)	4.50
$CaCl_2$ (mmol/L)	1.50
$MgSO_4$ (mmol/L)	1.20
NaCl (mmol/L)	116.00
$NaHCO_3$ (mmol/L)	25.00
NaH_2PO_4 (mmol/L)	0.80
Heparin (mg/L)	6.00
Glucose (mmol/L)	15.00
Insulin (U/L)	0.40
pCO_2 (mm Hg)	<40
pO_2 (mm Hg)	>750
pH	7.45
Osmolarity (mOsm/L)	290–310
Glycine (mg/L)	25.24
Lysine (mg/L)	69.23
Valine (mg/L)	22.03
L-Alanine (mg/L)	29.05
L-Arginine (mg/L)	20.73
L-Asparagine (mg/L)	8.99
L-Aspartic acid (mg/L)	1.86
L-Cysteine (mg/L)	7.88
L-Glutamic acid (mg/L)	17.65
L-Glutamine (mg/L)	95.27
L-Histidine (mg/L)	44.97
L-Isoleucine (mg/L)	14.17
L-Leucine (mg/L)	21.77
L-Methionine (mg/L)	8.05
L-Phenylalanine (mg/L)	11.40
L-Proline (mg/L)	12.43
L-Serine (mg/L)	25.96
L-Threonine (mg/L)	24.17
L-Tryptophan (mg/L)	10.21
L-Tyrosine (mg/L)	12.50
Cardioplegia solution	
NaCl (mmol/L)	77.0
KCl (mmol/L)	26.0
$CaCl_2$ (mmol/L)	0.05
$NaHCO_3$ (mmol/L)	22.0
pO_2 (mm Hg)	>750
pCO_2 (mm Hg)	<40
Glucose (g/L)	25.0
Mannitol (g/L)	12.5
Lidocaine (mg/L)	200.0
Nitroglycerin (mg/L)	0.5
pH	7.45
Osmolarity (mOsm/L)	360–380

Ischemic injury was induced by clamping the left atrial cannula and perfusing the aortic root with 20 mL of NIH No. 1 hyperkalemic cardioplegia solution (see Table 1) at a pressure of 80 cm H_2O. The hearts were given cardiople-

Table 2. Average Values of Rat Heart Nucleotides Before Ischemic Arrest[a]

Time	n	[NAD]	[AMP]	[ADP]	[ATP]
Frozen in chest	5	5.84 ± 0.50	3.92 ± 2.17	9.93 ± 2.48	32.96 ± 2.67
Excised and frozen	6	5.16 ± 0.22	2.33 ± 0.19	10.58 ± 0.86	30.78 ± 0.63
After 1 minute of perfusion	6	5.57 ± 0.35	2.37 ± 0.47	11.67 ± 1.16	36.13 ± 1.58
After 5 minutes of perfusion	10	6.38 ± 0.29	3.54 ± 0.50	13.39 ± 0.84	35.72 ± 2.01
After 15 minutes of perfusion	9	8.32 ± 0.34	2.19 ± 0.50	11.33 ± 1.24	42.66 ± 2.20
After 15 minutes in working mode	8	7.46 ± 0.60	1.64 ± 0.18	10.10 ± 0.44	42.50 ± 1.90

[a] Values expressed as mean ± standard error of the mean.

ADP, adenosine diphosphate (μmol/g protein); AMP, adenosine monophosphate (μmol/g protein); ATP, adenosine triphosphate (μmol/g protein); NAD, nicotinamide adenine dinucleotide (μmol/g protein).

gia and maintained at 37°C for 25 minutes or were given 24°C cardioplegia and maintained at 24°C throughout a 93-minute ischemic period. During the period of ischemia the heart was vented through the left atrial cannula. The heart was reperfused with buffer solution through the aortic root for 15 minutes in the nonworking mode to allow for washout of metabolites and rewarming. The heart was then placed in the working mode and postischemic measurements were made after 20 minutes. The buffer solution was recirculated only when the heart was in the working mode. The beating heart was then frozen with stainless steel Wollenberger tongs previously cooled to −70°C in liquid nitrogen. The distal portion of the heart was crushed and stored at −70°C. Analysis for adenosine triphosphate (ATP), adenosine diphosphate, adenosine monophosphate, and nicotinamide adenine dinucleotide content were performed within 24 hours by high-performance liquid chromatography.

Heart tissue samples of 25 mg were pulverized and homogenized in 6% perchloric acid at 0°C. After 30 minutes of extraction at 0°C, the samples were centrifuged for 10 minutes at 10,000 rpm and 0°C. The supernatant was neutralized to pH 7.0 by addition of KOH. The resulting fluid was then centrifuged for 5 minutes at 10,000 rpm and 0°C. The supernatant was again drawn off and filtered through a 0.2-μm filter before nucleotide determination [19]. The protein pellets remaining after the perchloric acid extraction were solubilized by heating in 0.5 N NaOH at 90°C for 1 hour. After thorough mixing, the total intracellular soluble protein content was determined by the method of Lowry and associates [20].

Nucleotide analyses were carried out on a Waters 510 high-performance liquid chromatograph (Millipore Corp, Venture, CA) with a variable-wavelength ultraviolet detector set at 254 nm. The separation of 10-μL samples was performed on a Hypersel ODS C-18 150 × 4.6 mm reverse-phase column (Keystone Scientific, Inc, State College, PA) at an eluent flow rate of 1.0 mL/min. The elution technique consisted of a gradient of methanol in an ammonium phosphate buffer (75 mmol/L, pH 5.75), with an analysis time, including column regeneration, of 16 minutes. Values were expressed as μmol/g of total intracellular soluble protein. Standards of adenosine monophosphate, adenosine diphosphate, ATP, and nicotinamide adenine dinucleotide were obtained for calibration of sample nucleotides (Sigma Chemical Co, St. Louis, MO). High-performance liquid chromatography–grade ammonium phosphate was obtained from Fisher Scientific Company. All of the animals used received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Statistical Analysis

Each measured variable (aortic flow, coronary flow, heart rate, systolic pressure, mean pressure, and diastolic pressure) or calculated value (cardiac output, stroke volume, left ventricular stroke work, and left ventricular power) was determined three times approximately 1 minute apart just before ischemic arrest and again at the end of the experiment. The mean percent recovery of the preischemic values was determined for each heart and for each group of 6 hearts. All statistical analyses were performed on the percent recovery values. The determination of adenine nucleotides was performed twice for each sample and the percent recovery was determined. A group of control hearts, which were killed before ischemic arrest, provided the preischemic ATP values (Table 2). Significant intergroup interactions were subjected to one-way analysis of variance with Scheffé probability testing. Significance was determined at p less than 0.05. All data were expressed as the mean ± the standard error of the mean. Data analysis was performed using Ab-Stat Software (Anderson-Bell Corp, Parker, CO) and Excel (Microsoft Corp, Redmond, WA) on an IBM P/S 2 model 70 computer.

Results

Mortality was defined as a heart that did not have any aortic flow after ischemic arrest (excluding coronary flow) regardless of whether or not a systolic pressure or heart rate was maintained. The ischemia times of 25 and 93 minutes were chosen because preliminary research demonstrated that they would produce substantial ischemic injury. Eighty-four (83%) of the 101 hearts that received nicardipine (5 to 50 μg/kg) performed work after ischemic arrest whereas only 50% of the 24 hearts that did not receive nicardipine performed work after ischemic arrest. Twelve (92%) of the 13 hearts that received the optimal

Table 3. Percentage of Working Hearts After Ischemic Arrest

25 Minutes of Ischemia at 37°C				93 Minutes of Ischemia at 24°C			
[Nicardipine] (μg/kg)	n	No. Working[a]	% Working[a]	[Nicardipine] (μg/kg)	n	No. Working[a]	% Working[a]
0	13	6	46%	0	11	6	55%
5	6	6	100%	5	7	6	86%
10	8	6	75%	10	6	6	100%
20	7	6	86%	20	9	6	67%
25	6	6	100%	25	7	6	86%
30	6	6	100%	30	7	6	86%
40	8	6	75%	40	9	6	67%
50	9	6	67%	50	6	6	100%
100	9	0	0%	100	6	0	0%

[a] After ischemic arrest.

dose of nicardipine (25 μg/kg) performed work after ischemic arrest. Fifteen hearts were treated with 100 μg/kg of nicardipine and were excluded from analysis because this dose was clearly toxic in that none of the hearts could perform work before ischemic arrest (Table 3). Tables 4 and 5 show the average preischemic and postischemic cardiac functional variables after normothermic and hypothermic ischemic arrest. Tables 6 and 7 show the average percent recovery of preischemic values after normothermic and hypothermic ischemic arrest (Fig 1).

Progressive increases in postischemic hemodynamic function and ATP content were seen with incremental doses of nicardipine up to 25 μg/kg. Further increases in dosage caused decreased function, but postischemic function was still better than in the untreated groups. Specifically, pretreatment with 25 μg/kg significantly increased ($p < 0.05$) the percent recovery (compared with the nontreated group) of the following variables of cardiac function: systolic pressure (74% to 96% at 37°C, 76% to 90% at 24°C), aortic flow (49% to 82% at 37°C, 48% to 77% at 24°C), cardiac output (61% to 90% at 37°C, 62% to 84% at 24°C), stroke volume (66% to 93% at 37°C, 67% to 92% at 24°C), left ventricular power (48% to 92% at 37°C, 48% to 84% at 24°C), stroke work (49% to 95% at 37°C, 50% to

Table 4. Average[a] Function After 25 Minutes of Ischemic Arrest at 37°C

	Concentration of Nicardipine (μg/kg)							
Variable	0	5	10	20	25	30	40	50
HR								
Pre	270.8 ± 25.4	237.0 ± 9.1	238.3 ± 11.0	274.8 ± 21.2	235.3 ± 7.1	242.7 ± 13.5	255.0 ± 6.8	261.3 ± 10.1
Post	265.0 ± 30.9	221.0 ± 19.9	234.5 ± 14.2	262.8 ± 21.6	226.7 ± 6.7	220.8 ± 15.7	239.3 ± 11.1	250.7 ± 8.5
AF								
Pre	54.6 ± 4.7	50.0 ± 3.4	55.5 ± 2.1	53.4 ± 2.8	45.5 ± 1.4	49.0 ± 3.3	46.0 ± 1.5	51.4 ± 4.0
Post	25.6 ± 3.7	33.2 ± 2.6	41.6 ± 4.6	40.4 ± 2.0	37.2 ± 1.3	34.3 ± 2.3	28.3 ± 3.8	27.9 ± 4.8
CF								
Pre	17.6 ± 2.5	17.6 ± 1.3	20.1 ± 2.6	19.3 ± 2.2	17.6 ± 1.6	15.5 ± 1.7	19.7 ± 2.3	19.8 ± 1.0
Post	21.2 ± 2.4	17.5 ± 1.4	22.6 ± 3.7	21.9 ± 1.9	19.3 ± 1.9	17.5 ± 1.8	22.2 ± 5.6	21.0 ± 3.8
SP								
Pre	88.1 ± 10.8	99.2 ± 3.5	92.1 ± 3.3	90.0 ± 0.0	97.0 ± 9.6	95.0 ± 6.1	94.8 ± 3.2	107.8 ± 12.4
Post	64.6 ± 7.1	92.8 ± 3.8	84.1 ± 2.2	83.6 ± 2.0	92.9 ± 9.9	87.0 ± 10.1	85.6 ± 2.9	82.1 ± 8.6
DP								
Pre	48.0 ± 5.5	32.8 ± 2.9	37.3 ± 1.5	37.2 ± 1.2	39.3 ± 4.3	42.5 ± 2.4	37.1 ± 1.7	43.8 ± 5.2
Post	45.0 ± 4.3	37.7 ± 3.2	39.6 ± 1.4	40.5 ± 1.9	42.1 ± 3.6	45.5 ± 3.1	44.3 ± 4.2	47.6 ± 6.5
ATP								
Pre	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9
Post	34.9 ± 1.1	34.8 ± 0.9	37.5 ± 1.5	36.7 ± 2.3	39.5 ± 1.1	38.1 ± 0.2	33.9 ± 2.1	33.2 ± 0.6

[a] n = 6 hearts in each group. Values expressed as mean ± standard error of the mean.

AF = aortic flow (mL/min); ATP = adenosine triphosphate (μmol/g protein); CF = coronary flow (mL/min); DP = diastolic pressure (mm Hg); HR = heart rate (beats/min); pre = before ischemia; post = after ischemia; SP = systolic pressure (mm Hg).

Table 5. Average[a] Function After 93 Minutes of Ischemic Arrest at 24°C

	Concentration of Nicardipine (μg/kg)							
Variable	0	5	10	20	25	30	40	50
HR								
Pre	245.7 ± 13.2	252.0 ± 5.6	252.5 ± 90.8	249.6 ± 9.1	246.3 ± 14.1	239.3 ± 12.5	265.2 ± 11.0	268.0 ± 18.3
Post	235.2 ± 21.5	254.6 ± 8.3	246.6 ± 6.8	251.5 ± 11.2	231.7 ± 21.8	217.0 ± 18.7	238.9 ± 18.4	274.0 ± 34.5
AF								
Pre	57.6 ± 4.5	55.6 ± 4.2	56.1 ± 4.6	53.6 ± 4.9	51.7 ± 4.3	54.2 ± 4.0	53.6 ± 4.1	64.2 ± 6.3
Post	26.8 ± 2.0	32.9 ± 1.4	34.3 ± 3.2	39.3 ± 3.8	39.3 ± 3.2	33.2 ± 3.1	26.8 ± 3.1	32.8 ± 6.2
CF								
Pre	25.6 ± 4.2	22.1 ± 1.6	25.8 ± 3.2	22.1 ± 3.3	23.6 ± 1.4	23.2 ± 2.0	24.8 ± 2.1	25.9 ± 1.7
Post	22.0 ± 4.2	21.8 ± 2.2	30.1 ± 3.1	30.6 ± 6.6	23.6 ± 1.3	27.4 ± 8.0	25.7 ± 1.5	31.2 ± 6.3
SP								
Pre	93.1 ± 4.0	98.4 ± 2.6	84.3 ± 3.3	94.2 ± 4.7	93.4 ± 7.4	100.2 ± 5.5	92.3 ± 3.9	97.9 ± 2.9
Post	71.5 ± 6.8	86.2 ± 2.3	74.2 ± 3.9	81.8 ± 3.3	83.3 ± 4.9	86.0 ± 3.2	82.7 ± 5.7	83.7 ± 8.3
DP								
Pre	40.8 ± 8.5	33.8 ± 2.0	34.2 ± 4.9	37.0 ± 1.8	35.3 ± 2.4	35.7 ± 1.9	36.7 ± 1.9	36.1 ± 1.8
Post	33.7 ± 3.8	39.1 ± 1.4	49.2 ± 1.5	40.0 ± 1.4	40.0 ± 0.5	38.7 ± 1.8	37.7 ± 3.2	55.0 ± 2.5
ATP								
Pre	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9	45.5 ± 1.9
Post	26.6 ± 0.7	27.9 ± 1.9	28.2 ± 1.5	30.1 ± 0.5	31.3 ± 1.1	27.2 ± 0.6	26.0 ± 0.5	26.2 ± 0.8

[a] n = 6 hearts in each group. Values expressed as mean ± standard error of the mean.

AF = aortic flow (mL/min); ATP = adenosine triphosphate (μmol/g protein); CF = coronary flow (mL/min); DP = diastolic pressure (mm Hg); HR = heart rate (beats/min); pre = before ischemia; post = after ischemia; SP = systolic pressure (mm Hg).

92% at 24°C), and ATP (76% to 87% at 37°C, 58% to 68% at 24°C). There were no significant changes in heart rate, coronary flow, or diastolic pressure.

Comment

Calcium is an important intracellular regulatory cation that plays an essential role in the mechanics of excitation-contraction coupling and normally enters the cell through voltage-activated calcium channels, passive diffusion, or exchange with sodium [21]. Large calcium fluxes occur within the cell during each beat as a normal part of the contractile process; however excessive calcium entry into the cell during reperfusion can be highly deleterious. The exact mechanism for calcium entry into the cell during ischemia is not known, but it is set into motion during ischemia with the actual influx and damage occurring during reperfusion. The injury that occurs may be characterized in part by the loss of ATP stores, intracellular acidosis, free radical formation, and intracellular edema.

Table 6. Average[a] Percent Recovery of Function After 25 Minutes of Ischemic Arrest at 37°C

	Concentration of Nicardipine (μg/kg)							
Variable	0	5	10	20	25	30	40	50
HR	97 ± 6	93 ± 6	98 ± 4	94 ± 2	96 ± 2	90 ± 3	94 ± 6	96 ± 5
AF	49 ± 7	68 ± 7[b]	74 ± 6[b]	74 ± 3[b]	82 ± 3[b]	70 ± 2[b]	60 ± 6	53 ± 6
CF	106 ± 6	100 ± 6	109 ± 7	104 ± 4	110 ± 5	113 ± 4	110 ± 25	100 ± 25
SP	74 ± 5	93 ± 3[b]	91 ± 1[b]	91 ± 1[b]	96 ± 2[b]	91 ± 5[b]	90 ± 3[b]	76 ± 1
DP	98 ± 11	116 ± 7	106 ± 1	99 ± 1	109 ± 5	108 ± 8	118 ± 7[b]	100 ± 2
CO	61 ± 7	76 ± 6[b]	83 ± 5[b]	82 ± 2[b]	90 ± 4[b]	80 ± 1[b]	76 ± 1	69 ± 5
SV	66 ± 12	83 ± 7	85 ± 5	88 ± 2[b]	93 ± 5[b]	89 ± 2[b]	80 ± 8	73 ± 8
LVSW	49 ± 4	87 ± 8[b]	82 ± 6[b]	86 ± 2[b]	95 ± 6[b]	87 ± 2[b]	82 ± 8[b]	62 ± 6[b]
LVP	48 ± 6	79 ± 4[b]	81 ± 5[b]	81 ± 2[b]	92 ± 5[b]	79 ± 2[b]	78 ± 10[b]	59 ± 5
ATP	76 ± 2	76 ± 1	81 ± 3[b]	82 ± 4	87 ± 2[b]	83 ± 0[b]	74 ± 5	74 ± 1

[a] n = 6 hearts in each group. Values expressed as mean ± standard error of the mean. [b] Significantly increased from nontreated group ($p < 0.05$).

AF = aortic flow; ATP = adenosine triphosphate; CF = coronary flow; CO = cardiac output; DP = diastolic pressure; HR = heart rate; LVSW = left ventricular stroke work; LVP = left ventricular power; SP = systolic pressure; SV = stroke volume.

Table 7. Average[a] Percent Recovery of Function After 93 Minutes of Ischemic Arrest at 24°C

	Concentration of Nicardipine (μg/kg)							
Variable	0	5	10	20	25	30	40	50
HR	95 ± 7	99 ± 3	98 ± 3	100 ± 3	93 ± 4	91 ± 9	90 ± 3	101 ± 8
AF	48 ± 5	60 ± 3^b	62 ± 5^b	74 ± 3^b	77 ± 1^b	61 ± 2^b	51 ± 5	51 ± 9
CF	97 ± 7	105 ± 4	126 ± 19	133 ± 8	110 ± 3	112 ± 23	105 ± 6	117 ± 17
SP	76 ± 5	87 ± 4^b	88 ± 2^b	86 ± 2^b	90 ± 3^b	87 ± 4^b	89 ± 4^b	84 ± 6^b
DP	94 ± 15	113 ± 6	119 ± 16	109 ± 3	116 ± 9	108 ± 1	102 ± 7	113 ± 6
CO	62 ± 7	71 ± 3^b	82 ± 7^b	92 ± 3^b	84 ± 1^b	77 ± 8^b	68 ± 5	72 ± 12
SV	67 ± 12	72 ± 4^b	83 ± 5^b	91 ± 3^b	92 ± 5^b	87 ± 11^b	76 ± 6^b	72 ± 11
LVSW	50 ± 4	69 ± 6^b	80 ± 7^b	86 ± 4^b	92 ± 7^b	82 ± 13^b	71 ± 7^b	68 ± 10
LVP	48 ± 6	69 ± 6^b	79 ± 9^b	86 ± 3^b	84 ± 3^b	72 ± 10^b	63 ± 6^b	66 ± 10^b
ATP	58 ± 1	61 ± 4	62 ± 3	66 ± 1^b	68 ± 2^b	61 ± 1	57 ± 1	57 ± 2

[a] n = 6 hearts in each group. Values expressed as mean ± standard error of the mean. [b] Significantly increased from nontreated group ($p < 0.05$).

AF = aortic flow; ATP = adenosine triphosphate; CF = coronary flow; CO = cardiac output; DP = diastolic pressure; HR = heart rate; LVSW = left ventricular stroke work; LVP = left ventricular power; SP = systolic pressure; SV = stroke volume.

All of these disrupt the normal internal milieu of the cell leading to damage on reperfusion. The reperfusion changes result in depressed myocardial function, massive tissue disruption, enzyme release, and development of contracture [2, 4]. The damage that occurs during the calcium paradox (severe cellular damage occurring after the introduction of calcium after a calcium-free perfusion period) is probably only a more severe form of the damage that occurs after ischemic arrest in the presence of calcium.

Recovery of preischemic function is dependent on many factors, which include the dose of calcium antago-

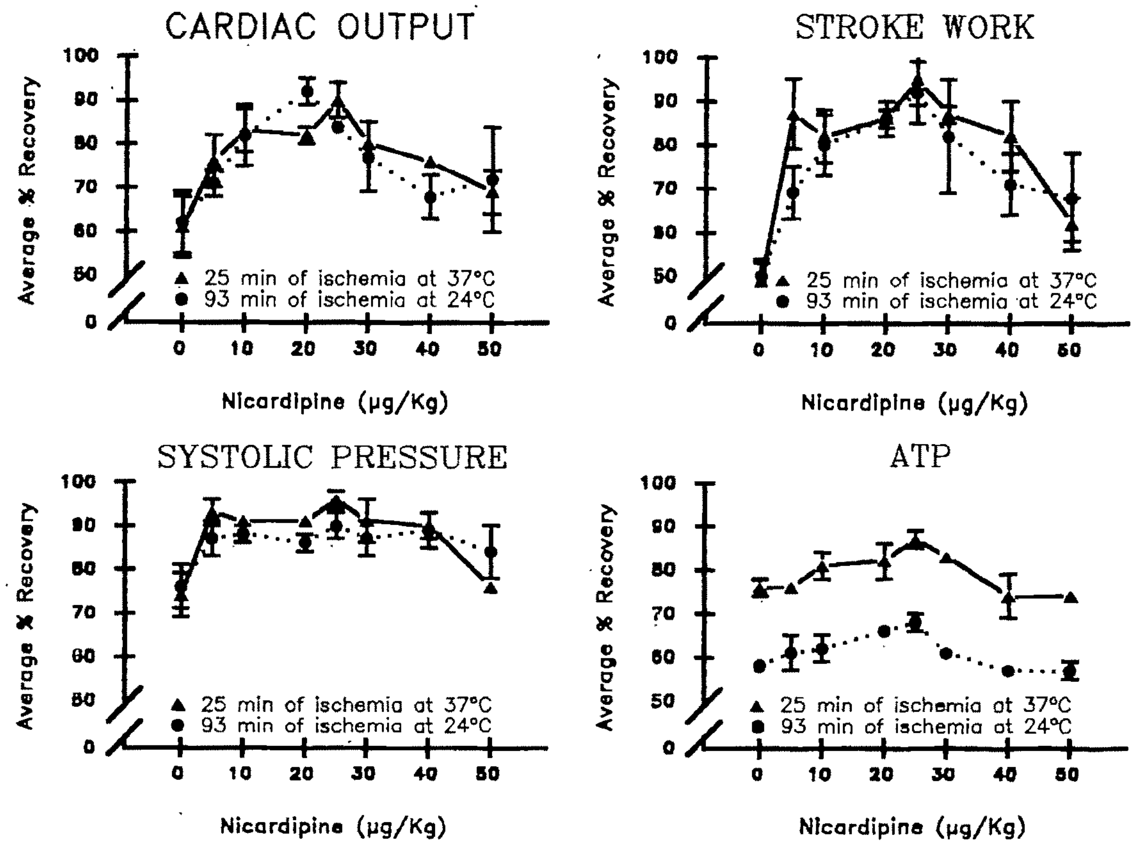

Fig 1. Percent recovery of preischemic values after the administration of normothermic (37°C) and hypothermic (24°C) cardioplegia (n = 6 for each point). Cardiac output, left ventricular stroke work, systolic pressure, and adenosine triphosphate (ATP) *concentration all increased* ($p < 0.05$) *when comparing groups with 0 versus 25 μg/kg nicardipine at 37° and 24°C.*

nist, time of administration, temperature during ischemic arrest, and the calcium concentration in the cardioplegic and reperfusate solutions. The results of this study show significant progressive increases in postischemic myocardial performance after ischemic arrest at 37° and 24°C. The protective effects of pretreatment with up to 25 μg/kg of nicardipine were not masked, but were additive to those of hypothermia. Similar beneficial effects on postischemic ventricular function at 37°C only have been demonstrated with administration of calcium antagonists such as verapamil [9, 22], nifedipine [10, 22], and also with nicardipine [7].

Bersohn and Shine [9] showed that pretreatment with a calcium antagonist 4 minutes before the onset of ischemia increased myocardial protection although administration 10 minutes after the onset of ischemia afforded no additional protection at 37°C. Cardioplegic solutions containing verapamil [6] or nifedipine [8, 10] do not afford any additional protection over hypothermia alone if infused at less than 32° and 28°C, respectively. The recovery of postischemic function is also inversely related to the calcium content of the cardioplegia solution [1] and the reperfusate [5]. The absence of protection by nicardipine in a cardioplegic solution after ischemic arrest below 32°C was also confirmed in this laboratory. However pretreatment with nicardipine showed significant improvements over hypothermia (>23°C) alone. Funkumi and Hearse [10] postulated that there was a common mechanism to both hypothermia and the action of calcium antagonists, which render each other redundant, and that calcium antagonists and hypothermia act by inducing conformational changes of the cellular membrane to prevent cellular damage. Because a beneficial effect is shown with pretreatment and hypothermia, there must be other factors at work.

The most plausible explanation for the mechanism of calcium entry into the cell during ischemia has been proposed by Tani and Neeley [23]. During cardioplegic arrest mechanical contraction of the sarcomere is not needed; however, continued operation of the sodium-potassium exchange membrane pump requires the presence of ATP. As ATP is utilized and production is slowed during ischemia, decreased activity of the membrane pump results. Intracellular sodium increases during ischemia, hence the higher the calcium concentration in the reperfusate solution the higher the exchange of intracellular sodium for calcium and the more the resulting cellular injury. Dichlorobenzamil, which is a blocker of this pump, reduced the calcium influx significantly when given during a 30-minute reperfusion period [24], and vascular washout of calcium by low-flow perfusion improves postischemic function by preventing calcium overload during reperfusion [3]. Furthermore mitochondria overloaded with calcium during ischemia have a decreased ability to produce ATP [22]. Excessive calcium entry through the Na^+/Ca^{2+} exchange pump is one of the major factors that determine the recovery of function during reperfusion, but calcium antagonists are not known to have a direct effect on this pump. These agents may act in other ways to conserve ATP to prevent the accumulation of intracellular sodium.

Few clinical trials with calcium antagonists as an adjunct to cardioplegia have been published, but with generally positive results. Clark and associates [11] reported on the first clinical trial of cardioplegia solution containing nifedipine. There was a twofold increase postoperatively in cardiac index and stroke work, and a 50% decrease of low cardiac output–related death in a group of 205 high-risk patients with the use of hypothermic cardioplegia solution containing nifedipine. Weinstein and co-workers [12] "pretreated" patients with verapamil before aortic cross-clamping and showed a 28% reduction in infarct size in patients undergoing coronary artery bypass operations. Mori and colleagues [13] reported on the first clinical trial of hypothermic cardioplegia containing nicardipine in 20 pediatric patients in which early postoperative myocardial function was increased with a reduction of enzyme loss, and Barner and associates [17] demonstrated that hypothermic diltiazem cardioplegia preserved high-energy phosphates, improved postoperative myocardial metabolism, and reduced ischemic injury after elective coronary bypass. In the clinical setting, calcium antagonists provide increased postischemic myocardial preservation and do so under hypothermic conditions. The beneficial actions under hypothermic conditions in patients are explained by prevention of additional calcium influx and under hypothermic ischemic arrest by protection of local "hot spots" that occur during the continued cooling and rewarming of the heart. Additionally, calcium antagonists also increase coronary flow providing better distribution of cardioplegia and reduce peripheral vascular resistance resulting in reduced afterload.

Calcium antagonists vary in ability to provide increased myocardial protection under hypothermic conditions. This study demonstrated that pretreatment of the heart with nicardipine enhanced myocardial protection at lower temperatures than when given in the cardioplegic solution only. Pretreatment could possibly raise the efficacy of other calcium channel blockers at lower temperatures. Calcium antagonists in general provide beneficial improvements in postischemic function and should not be discontinued and should probably be started before cardiac operations to minimize the risk of a preoperative ischemic event, but also to provide some degree of additional postischemic myocardial preservation.

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References

1. Geffin GA, Love TR, Henderen WG, et al. The effects of calcium and magnesium on myocardial preservation. J Thorac Cardiovasc Surg 1989;98:239–50.
2. Shen AC, Jennings RB. Myocardial calcium and magnesium in acute ischemic injury. Am J Pathol 1972;67:454–71.

3. Tani M, Neeley JR. Vascular washout reduces Ca^{2+} overload and improved function of reperfused ischemic hearts. Am J Physiol 1990;258:H354–61.
4. Hearse DJ, Humphrey SM, Bullock GR. The oxygen paradox and the calcium paradox: two facets of the same problem. J Mol Cell Cardiol 1978;10:641–68.
5. Hamaski T, Kuroda H, Mori T. Temperature dependency of calcium-induced reperfusion injury in the isolated rat heart. Ann Thorac Surg 1988;45:306–10.
6. Hearse DJ, Yamamoto F, Shattock MJ. Calcium antagonists and hypothermia: the temperature dependency of the negative inotropic and anti-ischemic properties of verapamil in the isolated rat heart. Circulation 1984;50:154–64.
7. Shikama H, Noshiro O, Ohata A, Ohhata I. Effects of nicardipine on ischemic mechanical failure and tissue injury in isolated perfused rat heart. Jpn Heart J 1985;26:813–21.
8. Nayler WG. Protection of the myocardium against postischemic reperfusion damage: the combined effect of hypothermia and nifedipine. J Thorac Cardiovasc Surg 1982;84: 897–905.
9. Bersohn MM, Shine KI. Verapamil protection of ischemic isolated rabbit heart: dependence on pretreatment. J Mol Cell Cardiol 1983;15:659–71.
10. Funkumi M, Hearse DJ. Temperature-dependence of nifedipine as a protective agent during cardioplegia in the rat. Cardiovasc Res 1985;19:95–103.
11. Clark RE, Magovern GJ, Christlieb IY, Boe S. Nifedipine cardioplegia experience: results of a 3 year cooperative clinical study. Ann Thorac Surg 1983;36:654–63.
12. Weinstein GS, Rao PS, Tyras DH. Reduction of myocardial injury with verapamil before aortic cross-clamping. Ann Thorac Surg 1990;49:419–23.
13. Mori F, Miuamoto M, Noda H, Esato K. Clinical trial of nicardipine cardioplegia in pediatric cardiac surgery. Ann Thorac Surg 1990;49:413–8.
14. Vouhe PR, Helias J, Grondin CM. Myocardial protection through cold cardioplegia using diltiazem, a calcium channel blocker. Ann Thorac Surg 1980;30:342–8.
15. Christakis GT, Fremes SE, Weisel RD, Tittley JG. Diltiazem cardioplegia. A balance of risk and benefit. J Thorac Cardiovasc Surg 1986;91:647–61.
16. Barner HB, Jellinek M, Standeven JW, Menz LJ, Hahn JW. Cold blood-diltiazem cardioplegia. Ann Thorac Surg 1982;33: 55–63.
17. Barner HB, Swartz MT, Devine JE, Williams GA, Janosik D. Diltiazem as an adjunct to cold blood potassium cardioplegia: a clinical assessment of dose and prospective randomization. Ann Thorac Surg 1987;43:191–7.
18. Neely JR, Leibermeister H, Battersby EJ, Morgan HE. Effect of pressure development on oxygen consumption by isolated rat heart. Am J Physiol 1967;212:804–16.
19. Sellevold OFM, Junge P, Aarstad K. High performance liquid chromatography: a rapid isocratic method for determination for creatine compounds and adenine nucleotides in myocardial tissue. J Mol Cell Cardiol 1986;18:517–27.
20. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem 1951;193:265–75.
21. De Jong JW. Cardioplegia and calcium antagonists. Ann Thorac Surg 1986;42:593–8.
22. Nayler WG, Ferrari R, Williams A. Protective effect of pretreatment with verapamil, nifedipine and propranolol on mitochondrial function in the ischemic and reperfused myocardium. Am J Cardiol 1980;48:242–8.
23. Tani M, Neely JR. Mechanisms of reduced reperfusion injury by low Ca^{2+} and/or high K^+. Am J Physiol 1990;258(Heart Circ Physiol 27):1025–31.
24. Murphy JD, Smith TW, March JD. Role of Na/Ca exchange in reoxygenation induced calcium overload in cultured heart cells. Circulation 1986;749(Suppl 2):83–9.

Six Different Hemofiltration Devices for Blood Conservation in Cardiac Surgery

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Hemofiltration devices and the Cell Saver are the most often used techniques to reduce homologous blood requirements in cardiac surgery. In a controlled, randomized study, 105 patients underwent elective aortocoronary bypass grafting. Six different hemofilters (HF-80, HFT 14, CPB 7000, Cobe 1200, UF-205, BC-140) were tested and compared with the Cell Saver (Cell Saver 4) for blood concentration during and after cardiopulmonary bypass. Efficacy, practicality, and laboratory indices including coagulation variables were documented through the morning of the first postoperative day. The HF-80 and UF-205 were the most effective devices for blood concentration. At the end of the operation, the number of platelets was least reduced in these two groups (HF-80, −7%; UF-205, −6%). Moreover, both devices had a significantly higher filtration rate than the other hemofilters. Use of the Cell Saver resulted in the lowest values in coagulation variables (AT-III, fibrinogen, number of platelets) and the most pronounced deterioration in protein homeostasis (colloid osmotic pressure, albumin). In this group, the AT-III concentration was reduced until the morning of the first postoperative day. No negative effects were seen in regard to hemofiltration (free hemoglobin and polymorphonuclear elastase; the Cell Saver group had similar values for these variables). We conclude that blood salvage with hemofiltration devices is superior to that with the Cell Saver. There were, however, significant differences among the hemofilters. The HF-80 and UF-205 were the most effective devices in this study.

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Transfusion of homologous blood is still associated with the risk of transferring viral diseases [1, 2]. In the United States, more than 1,500 deaths are due to posttransfusion hepatitis and the number of cases of acquired immunodeficiency syndrome resulting from a transfusion is unknown. Blood transfusion practices have been placed under increasing scrutiny [3]. Moreover, the shortage of blood donors has led to a growing interest in blood conservation techniques.

In the past, blood use was great in cardiac operations [4]. Several strategies used separately or together may help reduce the need for transfusion of homologous blood or blood derivatives. These techniques include preoperative hemodilution, asanguineous priming of the heart-lung machine, and application of substances such as aprotinin that might preserve coagulation [5, 6].

The two most common methods are the Cell Saver and hemofiltration devices, which are used during and after cardiopulmonary bypass (CPB) [7–12]. In contrast to the cell saver technique, hemofiltration has the advantage of removing only the excessive fluids from the blood while completely preserving plasma proteins, which are wasted by the centrifugation technique. Various hemofiltration devices made of different membrane materials and having different membrane surface areas are available. To date, the ideal device for hemoconcentration in cardiac surgical procedures remains unknown. This study was designed to examine six different hemofiltration devices in regard to efficacy, practicality, and certain laboratory variables and to compare them with the Cell Saver.

Material and Methods

Patients and Grouping

The study group comprised 105 patients undergoing elective aortocoronary bypass grafting. Informed consent was obtained from each patient according to the protocol of the Human Ethics Committee of the hospital. Criteria excluding participation in the study were premedication with heparin sodium, aspirin, or adenyl cyclase inhibitors and preoperative coagulation abnormalities.

The patients were randomly divided into seven groups in which six different hemofilters and one Cell Saver were used for hemoconcentration during and after CPB. The seven groups, each with 15 patients, were as follows:

Group 1: HF-80 (Fresenius, Bad Homburg, FRG): membrane material, polysulfone; surface area, 1.80 m^2
Group 2: Spiraflow HFT 14 (Sorin, Torino, Italy): membrane material, polysulfone; surface area, 1.35 m^2
Group 3: CPB 7000 (Bentley Laboratories, Irvine, CA). membrane material, polyacrylonitrile; surface area, 1.00 m^2

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Group 4: Cobe 1200 (Cobe Laboratories, Heimstetten, FRG): membrane material, polyacrylonitrile; surface area, 1.20 m^2
Group 5: UF-205 (Nipro, Japan): membrane material, triacetate; surface area, 1.70 m^2
Group 6: BC-140 (Gambro, Munich, FRG): membrane material, polyamide; surface area, 1.40 m^2
Group 7: Cell Saver 4 (Haemonetics, Munich, FRG)

Technique of Hemofiltration

Five minutes after the start of CPB, blood in the extracorporeal circuit was concentrated by the hemofiltration technique. Blood was taken from the venous reservoir and pumped through the hemofilter to the cardiotomy reservoir at a flow of 500 mL/min. No vacuum suction was used. Inlet and outlet pressures of the hemofilters during filtration were monitored, as was the time necessary to remove 500 mL of ultrafiltrate. During CPB, we attempted to keep the volume of ultrafiltrate identical to the volume of cardioplegic solution. After CPB, the blood remaining in the extracorporeal oxygenation equipment was pumped once through the hemofiltration device (single-pass ultrafiltration) at the same flow rate, 500 mL/min. The concentrated blood was collected and weighed before retransfusion (hemofiltration blood).

Anesthesia and Cardiopulmonary Bypass

Induction and maintenance of anesthesia were comparable for all groups and consisted of weight-related doses of fentanyl, midazolam hydrochloride, and pancuronium bromide. All patients were on controlled mechanical ventilation perioperatively and during the first 5 hours postoperatively. The ratio of arterial oxygen tension to inspired oxygen fraction was calculated for better statistical interpretation.

Anticoagulation was achieved by administration of 300 U/kg of heparin 5 minutes before the start of CPB. Cardiopulmonary bypass was carried out with a nonpulsatile pump and a Sorin 41 membrane oxygenator. The circuit was primed with 1,000 mL of 5% dextrose, 1,000 mL of Ringer's solution, 250 mL of 5% albumin, and electrolytes. A perfusion flow of 2.4 L/min · m^2 was maintained throughout the entire bypass period, and moderate hypothermia (lowest esophageal temperature, 33.2° ± 1.0°C) was used during CPB. A two-stage cannula was used for venous return into the circuit (the monoatrial cannulation technique). With this technique, all cardioplegic solution (1,000 mL of Bretschneider solution) is returned to the extracorporeal circuit.

Within 20 minutes after the start of CPB, blood in the circuit was concentrated using one of the hemofiltration devices or the Cell Saver. The amount of ultrafiltrate removed from the circuit by the device equaled the amount of cardioplegic solution used for myocardial preservation. When necessary in the later part of bypass, Ringer's solution was added to the heart-lung machine to guarantee an adequate filling volume. When hemoglobin concentration was less than 70 g/L (7 g/dL), packed red cells were given. During weaning from bypass, as much pump blood as necessary to keep pulmonary capillary wedge pressure between 10 and 12 mm Hg was infused. After the termination of CPB, the residual blood in the circuit (pump blood) was salvaged by the same techniques as already described, and the concentrated blood (hemofiltration blood or Cell Saver blood) was retransfused until the end of the operation. Protamine sulfate was given in the same dose as the initial dose of heparin.

Laboratory Studies and Data Points

The following variables were measured from arterial blood samples: hemoglobin; hematocrit; number of red and white blood cells; number of platelets; free hemoglobin; blood gas variables (ratio of arterial oxygen tension to inspired oxygen fraction); colloid osmotic pressure (Sartorius membrane, 20,000 dalton); total protein; albumin; coagulation variables (thrombin time, prothrombin time, partial thromboplastin time, activated clotting time, thrombelastogram); heparin concentration; fibrinogen; AT-III; electrolytes (Na^+, K^+); and polymorphonuclear elastase. Blood samples were taken at six time points: before the start of CPB; 30 minutes after the start of CPB (after hemoconcentration was completed); immediately after the termination of CPB (before application of washed erythrocytes and protamine); at the end of the operation (after retransfusion of hemofiltration blood or Cell Saver blood); 5 hours after the end of the operation; and on the morning of the first postoperative day.

In addition to measurements from patients' blood, samples were taken from hemofiltration blood and Cell Saver blood after CPB. Fluid balance during CPB (input and output including blood loss), blood loss from chest tube drainage, and volume in the postoperative period (Ringer's solution when the pulmonary capillary wedge pressure was less than 8 mm Hg; packed red cells when the hemoglobin value was less than 90 g/L [9 g/dL]) were also documented. All volumes were infused by anesthesiologists who were not involved in the study.

Statistical Analysis

The results are expressed as the mean ± the standard deviation. Multiple testing of one-factor and two-factor analyses of variance followed by Scheffé tests were used for statistical interpretation. Significance was defined as a p value of less than 0.05.

Results

The seven groups were comparable in regard to biometric data and duration of CPB and ischemia (Table 1). Fluid balance during CPB, however, was significantly greater in the Cell Saver group than in all the hemofiltration groups (see Table 1). Patients with the HF-80 and UF-205 showed the lowest fluid balances after CPB. Blood loss through the morning of the first postoperative day was most pronounced in the Cell Saver group (690 ± 180 mL) (see Table 1). Infusion of packed red cells was necessary only in the HFT 14, CPB 7000, Cobe 1200, and Cell Saver groups (see Table 1).

Table 1. Summary of Patient Data and Operative Data[a]

	Hemofiltration Device						
Variable	HF-80	HFT 14	CPB 7000	Cobe 1200	UF-205	BC-140	Cell Saver
Age (y)	65.2 ± 8.8	58.3 ± 7.0	58.6 ± 9.7	62.6 ± 9.1	58.8 ± 9.0	60.8 ± 9.7	58.4 ± 6.6
Weight (kg)	76.4 ± 11.9	77.2 ± 11.1	80.3 ± 10.0	73.9 ± 5.8	75.4 ± 6.6	76.7 ± 11.9	73.2 ± 6.9
CPB (min)	75.3 ± 12.6	69.3 ± 10.1	66.3 ± 14.1	63.7 ± 11.1	69.0 ± 12.1	74.2 ± 16.2	68.3 ± 12.8
Ischemia (min)	44.1 ± 11.9	44.3 ± 9.1	40.7 ± 9.7	42.5 ± 12.1	43.6 ± 7.8	45.1 ± 7.8	44.3 ± 8.9
Fluid balance during CPB (mL)	80 ± 200[b]	280 ± 250	380 ± 220	450 ± 260	170 ± 260[b]	350 ± 160	850 ± 360[c]
Blood loss (mL)							
5 hours postop	160 ± 70	180 ± 90	250 ± 190	150 ± 60	180 ± 110	210 ± 120	380 ± 120
Postop day 1	390 ± 160	530 ± 300	420 ± 240	390 ± 80	360 ± 190	450 ± 200	690 ± 180[c]
Volume to postop day 1 (mL)							
Packed red cells (U/patients)	0/0	3/2	1/4	1/2	0/0	0/0	3/2
Ringer's solution (mL)	1,500 ± 330	1,890 ± 610	2,070 ± 850	1,800 ± 400	1,600 ± 400	1,790 ± 570	1,860 ± 410

[a] Where applicable, data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ versus the other hemofiltration groups. [c] Significance: $p < 0.05$ versus all the hemofiltration groups.

CPB = cardiopulmonary bypass.

The characteristics of the blood produced by the Cell Saver and the hemofiltration devices were different (Table 2). The hemoglobin level was lowest in the CPB 7000 and Cobe 1200 groups, but all important coagulation variables were significantly lower in the Cell Saver group compared with all the hemofiltration groups. Removal of 500 mL of ultrafiltrate was done most quickly by the HF-80 (2.75 ± 0.46 minutes) and the UF-205 (2.94 ± 0.51 minutes) (see Table 2). The CPB 7000, Cobe 1200, and Cell Saver needed the longest period. Input pressures were significantly lower for the HF-80 and the UF-205.

Table 3 demonstrates the most important changes in laboratory data for five time points. The major changes in laboratory variables immediately after CPB and at the end of the operation are illustrated in Figures 1 through 4.

Hemoconcentration was least effective in the CPB 7000 and Cobe 1200 patients, who had the lowest hemoglobin values at the end of the operation after retransfusion of the hemofiltration blood. At the end of the operation, the number of platelets was highest in the HF-80 and UF-205 patients and lowest in the Cell Saver patients, even 5 hours after the end of the operation. The AT-III concentration was also lowest in these patients, even on the morning of the first postoperative day. There were no differences between the groups in regard to polymorphonuclear elastase, heparin concentration, and free hemoglobin values. Global coagulation variables (thrombin time, prothrombin time, partial thromboplastin time, activated clotting time, thrombelastogram) and electrolytes were comparable for all groups during the entire study period.

Immediately after CPB and at the end of the operation, colloid osmotic pressure and albumin were significantly

Table 2. Laboratory Data From Salvaged Blood After Cardiopulmonary Bypass and Operative Data[a]

	Hemofiltration Device						
Variable	HF-80	HFT 14	CPB 7000	Cobe 1200	UF-205	BC-140	Cell Saver
Hemoglobin (g/L)	166 ± 22	158 ± 12	121 ± 13[b]	130 ± 22[b]	163 ± 20	134 ± 14[b]	162 ± 18
COP (mm Hg)	48.0 ± 10.9[b]	36.5 ± 10.0	24.4 ± 6.0[b]	38.4 ± 9.2	50.1 ± 8.8[b]	36.5 ± 10.5	1.6 ± 1.2[c]
AT-III (g/L)	0.39 ± 0.04	0.31 ± 0.04	0.25 ± 0.06[b]	0.24 ± 0.03[b]	0.37 ± 0.07	0.32 ± 0.12	0.11 ± 0.16[c]
Fibrinogen (g/L)	4.87 ± 1.77	4.61 ± 1.51	3.91 ± 1.58[b]	3.54 ± 1.00[b]	4.52 ± 1.68	4.06 ± 1.74	0.45 ± 0.15[c]
Platelets (10^9/L)	247 ± 52	248 ± 114	240 ± 81	194 ± 87[b]	258 ± 87	215 ± 62	50 ± 23[c]
PMN elastase (μg/L)	485 ± 229	598 ± 334	589 ± 419	642 ± 378	733 ± 332	614 ± 277	101 ± 78[c]
Free hemoglobin (mg/dL)	228 ± 79	203 ± 78	154 ± 36	169 ± 50	245 ± 98	174 ± 79	27 ± 10[c]
Time to remove ultrafiltrate, 500 mL (min)	2.75 ± 0.46[b]	4.02 ± 0.97	7.06 ± 1.36	7.36 ± 1.22	2.94 ± 0.51[b]	4.44 ± 0.67	7.10 ± 1.33
Concentrated blood (mL)	940 ± 150	1,050 ± 200	1,360 ± 130[b]	1,200 ± 120[b]	1,140 ± 200	1,260 ± 140	790 ± 140[c]
Ultrafiltrate removed after CPB (mL)	1,000 ± 200	900 ± 110	750 ± 190[b]	650 ± 150[b]	1,000 ± 160	900 ± 120	1,500 ± 200[c]

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ versus the other hemofiltration groups. [c] Significance: $p < 0.05$ versus all the hemofiltration groups.

COP = colloid osmotic pressure; CPB = cardiopulmonary bypass; PMN = polymorphonuclear.

Table 3. Changes in Laboratory Data for Five Time Points[a]

Variable	Group	Before CPB	After CPB	End of Operation	5 Hours Postop	Postop Day 1
Hemoglobin (g/L)	HF-80	130 ± 18	98 ± 12	118 ± 09	125 ± 12	128 ± 13
	HFT 14	132 ± 11	99 ± 10	116 ± 12	127 ± 15	115 ± 13
	CPB 7000	122 ± 11	92 ± 08	105 ± 13[b]	120 ± 14	111 ± 14
	Cobe 1200	125 ± 13	90 ± 11	104 ± 12[b]	112 ± 16	111 ± 13
	UF-205	128 ± 16	98 ± 09	117 ± 09	124 ± 13	114 ± 16
	BC-140	126 ± 09	95 ± 06	114 ± 13	119 ± 15	114 ± 09
	Cell Saver	129 ± 14	96 ± 14	122 ± 15	126 ± 24	124 ± 17
Colloid osmotic pressure (mm Hg)	HF-80	18.7 ± 2.9	13.2 ± 1.6	16.8 ± 2.5	20.3 ± 3.0	20.5 ± 3.4
	HFT 14	20.4 ± 1.9	12.5 ± 1.5	17.8 ± 2.4	22.8 ± 3.4	22.4 ± 3.6
	CPB 7000	19.3 ± 1.3	13.4 ± 3.0	16.5 ± 1.8	22.0 ± 1.8	21.4 ± 1.3
	Cobe 1200	19.6 ± 1.8	12.3 ± 0.9	16.6 ± 1.3	23.0 ± 3.0	21.4 ± 3.2
	UF-205	18.8 ± 2.3	11.8 ± 2.0	16.9 ± 3.2	20.2 ± 3.6	20.5 ± 3.3
	BC-140	20.2 ± 2.3	13.2 ± 1.9	18.5 ± 1.9	23.0 ± 2.7	24.1 ± 2.8
	Cell Saver	20.7 ± 1.6	10.8 ± 2.1[c]	15.0 ± 0.7[c]	21.5 ± 3.0	21.2 ± 2.2
Platelets (10^9/L)	HF-80	230 ± 50	189 ± 54	199 ± 37[b]	204 ± 42	180 ± 51
	HFT 14	209 ± 33	158 ± 33	181 ± 47	201 ± 67	197 ± 53
	CPB 7000	202 ± 49	184 ± 51	184 ± 37	204 ± 42	190 ± 29
	Cobe 1200	225 ± 31	175 ± 39	171 ± 47	188 ± 47	169 ± 38
	UF-205	218 ± 58	193 ± 36	201 ± 42[b]	199 ± 53	185 ± 55
	BC-140	195 ± 50	182 ± 69	160 ± 34[b]	187 ± 47	195 ± 70
	Cell Saver	215 ± 37	168 ± 40[c]	140 ± 48[c]	170 ± 42[c]	170 ± 52
AT-III (normal: 0.20–0.40 g/L)	HF-80	0.24 ± 0.03	0.17 ± 0.01	0.21 ± 0.02	0.24 ± 0.02	0.24 ± 0.01
	HFT 14	0.24 ± 0.02	0.16 ± 0.02	0.21 ± 0.03	0.24 ± 0.03	0.23 ± 0.02
	CPB 7000	0.23 ± 0.04	0.16 ± 0.03	0.20 ± 0.03	0.24 ± 0.05	0.22 ± 0.06
	Cobe 1200	0.22 ± 0.02	0.15 ± 0.01	0.19 ± 0.01	0.22 ± 0.04	0.20 ± 0.03
	UF-205	0.24 ± 0.03	0.16 ± 0.02	0.21 ± 0.04	0.23 ± 0.04	0.22 ± 0.04
	BC-140	0.23 ± 0.04	0.16 ± 0.03	0.20 ± 0.02	0.22 ± 0.04	0.22 ± 0.04
	Cell Saver	0.22 ± 0.02	0.14 ± 0.03	0.16 ± 0.03[c]	0.15 ± 0.04[c]	0.18 ± 0.01[c]
PMN elastase (normal: 15–40 μg/L)	HF-80	54 ± 17	115 ± 53	204 ± 143	132 ± 77	102 ± 49
	HFT 14	52 ± 15	115 ± 44	159 ± 52	105 ± 15	90 ± 27
	CPB 7000	49 ± 14	146 ± 133	183 ± 111	125 ± 73	82 ± 25
	Cobe 1200	62 ± 25	120 ± 66	205 ± 120	140 ± 48	96 ± 37
	UF-205	52 ± 15	185 ± 140	248 ± 130	150 ± 64	107 ± 29
	BC-140	50 ± 12	120 ± 43	173 ± 32	125 ± 43	88 ± 19
	Cell Saver	50 ± 20	180 ± 124	184 ± 194	122 ± 43	91 ± 16
Free hemoglobin (normal: <40 mg/dL)	HF-80	36 ± 11	48 ± 23	70 ± 27	49 ± 16	38 ± 11
	HFT 14	54 ± 40	61 ± 41	76 ± 30	68 ± 27	46 ± 25
	CPB 7000	45 ± 16	39 ± 13	59 ± 14	56 ± 13	39 ± 16
	Cobe 1200	37 ± 12	41 ± 13	62 ± 20	50 ± 11	37 ± 9
	UF-205	37 ± 14	44 ± 19	74 ± 24	57 ± 21	36 ± 13
	BC-140	37 ± 12	51 ± 19	76 ± 29	62 ± 21	37 ± 15
	Cell Saver	52 ± 22	43 ± 22	54 ± 27	52 ± 14	32 ± 13

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ versus the other hemofiltration groups. [c] Significance: $p < 0.05$ versus all the hemofiltration groups.

reduced in the Cell Saver group (see Table 3; Figs 2, 4). The arterial oxygen tension was also most compromised in these patients (see Figs 2, 4). Five hours after the operation and on the first postoperative day, no other significant differences were noted between the groups.

None of the patients sustained sequelae attributable to the study.

Comment

Five major aspects have to be taken into account when evaluating the best method for hemoconcentration during and after CPB: efficacy; changes in laboratory variables, particularly coagulation and protein variables; side effects; practicality; and, last but not least, cost of the technique.

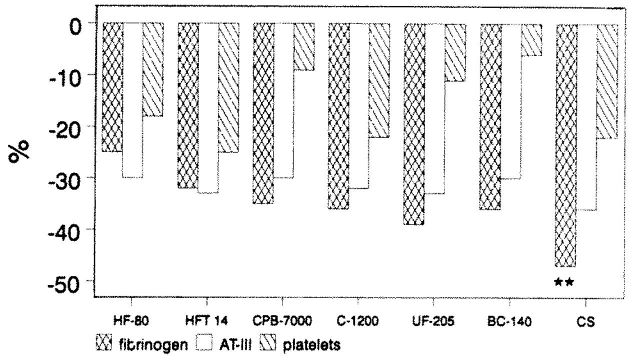

*Fig 1. Percent change in number of platelets and in AT-III and fibrinogen concentrations from before cardiopulmonary bypass (CPB) to the end of CPB. (C = Cobe; CS = Cell Saver; ** = $p < 0.05$ versus all the hemofiltration groups.)*

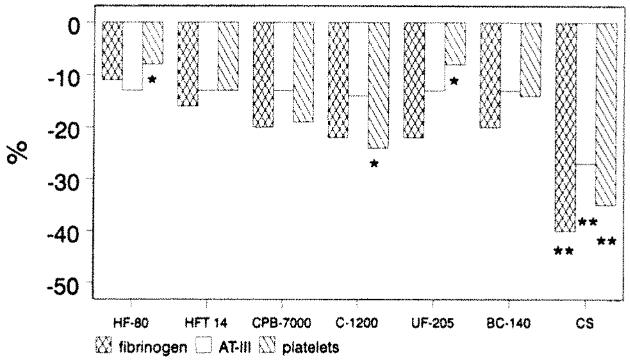

*Fig 3. Percent change in number of platelets and in AT-III and fibrinogen concentrations from before cardiopulmonary bypass to the end of the operation. (C = Cobe; CS = Cell Saver; * = $p < 0.05$ versus the other hemofiltration groups; ** = $p < 0.05$ versus all the hemofiltration groups.)*

In this study, the HF-80 and UF-205 hemofiltration devices were the most effective for hemoconcentration as well as improvement in coagulation and protein patterns. Less effective were the other hemofilters, though they were superior to the Cell Saver. Ultrafiltration differs substantially from centrifugation (the Cell Saver method). It effectively removes excess water while conserving and concentrating blood components and red blood cells. Removal of the plasma fraction is the biggest disadvantage when using the Cell Saver. In our study, this technique resulted in the lowest values of colloid osmotic pressure, albumin, number of platelets, and AT-III and fibrinogen concentrations at the end of the operation. The AT-III concentration was lowest in the Cell Saver patients even on the first postoperative day.

Use of the hemofiltration technique was not associated with any side effects. Retention of plasma including free hemoglobin and proteolytic enzymes such as polymorphonuclear elastase is speculated to be a negative aspect of this method [13], but this could not be confirmed by our study. Free hemoglobin values were always less than 100 μg/L in the patients with a hemofiltration device and were always comparable with data from studies in which no such devices were used [14]. Polymorphonuclear elastase, an important marker with respect to an activated white-cell system, increased in all patients, including the Cell Saver patients. Even in the hemofiltration patients, polymorphonuclear elastase was always less than 400 μg/L, a value found by other investigators [15] who did not use hemofiltration devices during and after CPB. Moreover, these values were far lower than those found in patients with a generalized inflammatory reaction, ie, in patients with sepsis [16]. Moreover, none of the hemofiltration patients experienced organ failure postoperatively. In the period after bypass, pulmonary function (arterial oxygen tension) in the hemofiltration was less compromised than in the Cell Saver patients, most likely because of the lower fluid balances and less impaired protein homeostasis (higher colloid osmotic pressure) in the former groups.

The controversy about the "ideal" material for the hemofiltration membrane is still unresolved [17]. Some objections against the use of hemofiltration in cardiac

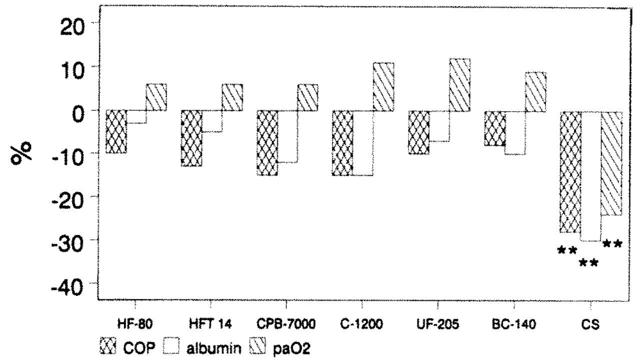

*Fig 2. Percent change in colloid osmotic pressure (COP), albumin, and arterial oxygen tension (paO_2) from before cardiopulmonary bypass (CPB) to the end of CPB. (C = Cobe; CS = Cell Saver; ** = $p < 0.05$ versus all the hemofiltration groups.)*

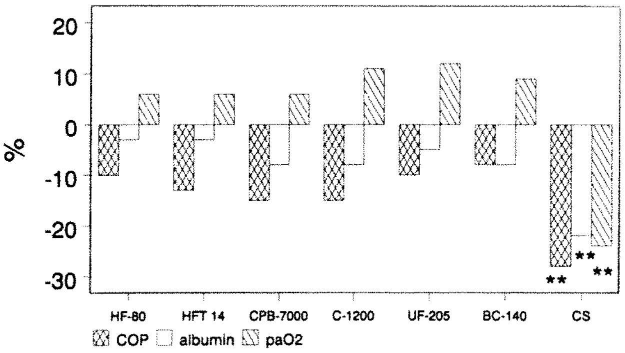

*Fig 4. Percent change in colloid osmotic pressure (COP), albumin, and arterial oxygen tension (paO_2) from before cardiopulmonary bypass to the end of the operation. (C = Cobe; CS = Cell Saver; ** = $p < 0.05$ versus all the hemofiltration groups.)*

surgery have been based on the fact that some types of membranes may cause additional complement activation and a decrease in leukocytes [18]. It has been demonstrated that these reactions occur mainly with membranes made of cellulose, cuprophane, and generated cellulose, whereas membranes made of polysulfone are less apt to have these effects.

From the practical point of view, all the hemofilters were easy to use during and after CPB. Each device was rinsed with Ringer's solution before use. It is, however, desirable that effective devices that do not require rinsing be available in the future to make handling much easier. The duration of the hemofiltration procedure was significantly different for the various devices used in this study. The HF-80 and UF-205 proved to be the quickest, most likely because of their large surface area. Thus, the filtration rate can be greatly enhanced by increasing the pump speed without the risk of reaching a critical filtration pressure. This may be of importance, particularly for hemoconcentration during CPB. In patients with congestive heart disease, it might be necessary to remove excessive water very fast. Previously we [20] reported that more than 4,000 mL of ultrafiltrate was removed in patients having operation on an emergency basis and in patients with severe congestive heart failure. This would not be advisable with the help of a Cell Saver, because a tremendous amount of plasma would also be removed.

After the completion of CPB, the HF-80 and UF-205 were the quickest hemofiltration devices as well. The autologous blood produced with the help of these devices can be retransfused early, thus reducing the need for homologous blood or asanguineous plasma substitutes, which might reduce hemoglobin concentration to a critical level. The Cell Saver technique was also far slower than these two hemofiltration devices because of its filling, washing, and returning procedure.

The question of whether one of the blood salvaging techniques (hemofiltration or the Cell Saver method) can contribute to reduced use of homologous blood is of highest importance. Because the number of patients in each group was small (n = 15), differences in infusion of packed red cells cannot be verified statistically. Overall, however, the patients treated with the hemofiltration devices needed fewer units of packed red cells (90 hemofiltration patients received 12 units versus 6 units in 15 Cell Saver patients). There were also differences in regard to transfused homologous blood among the hemofiltration groups. Moreover, since hemofiltration has become routine in our institution, infusion of blood products (fresh frozen plasma, platelets) has been drastically reduced.

Finally, costs associated with Cell Saver technique were higher than those for any of the hemofiltration devices. Although costs of medical equipment differ widely among countries, the cost of one Cell Saver was approximately 60% greater than that of the hemofiltration equipment. In addition, the cost of the centrifugation apparatus has to be considered.

We conclude that hemofiltration is becoming an established method for blood conservation in cardiac surgery. In parallel with CPB, it is a simple and effective procedure and a safe tool to accomplish hemoconcentration. Blood can be concentrated without negative effects in regard to coagulation and protein homeostasis. However, there were significant differences between the six hemofilters used in this study, a finding that emphasizes the fact that it is not the hemofiltration technique but the type of hemofilter used that determines the results. With respect to efficacy of blood concentration, changes in coagulation and protein variables, and practicality (ie, speed and input pressure), the HF-80 and UF-205 hemofiltration devices have proved to be the best in this situation. However, the ideal material for the membrane has yet to be determined.

References

1. Peterman TA. Transfusion-associated acquired immunodeficiency syndrome. World J Surg 1987;11:36–40.
2. Reesink HW, v d Poel CL. Blood transfusion and hepatitis: still a threat? Blut 1989;58:1–6.
3. Gravlee GP. Blood transfusion and component therapy. In: 1989 annual refresher course lectures. American Society of Anesthesiologists, 1989:164/1–7.
4. Lowenstein E. Blood conservation in open heart surgery. Cleve Clin Q 1981;3:112–25.
5. Angelini GD, Cooper GJ, Lamarra M, Bryan AJ. Unorthodox use of aprotinin to control life-threatening bleeding after cardiopulmonary bypass. Lancet 1990;335:799–800.
6. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
7. Nelson RL, Tamari Y, Tortolani AJ, Hall MH, Moccio CG. Ultrafiltration for concentration and salvage of pump blood. In: Utley JR, ed. Pathophysiology and technique of cardiopulmonary bypass; vol 2. Baltimore: Williams & Wilkins, 1983:229.
8. Solem JO, Tengborn L, Steen S, Luhrs C. Hemofiltration versus centrifugation for concentration of oxygenator residual content. J Cardiovasc Surg (Torino) 1987;35:42–7.
9. Magilligan DJ Jr, Oyama C. Ultrafiltration during cardiopulmonary bypass: laboratory evaluation and initial clinical experience. Ann Thorac Surg 1984;37:33–9.
10. Kinneberg PL, Kam CA, Johnson DC, Cartmill TB, Brown JH. Hematocrit and blood volume control during cardiopulmonary bypass with the use of hemofiltration. Anesthesiology 1984;60:478–80.
11. Mayer ED, Welsch M, Tanzeem A, et al. Reduction of postoperative donor blood requirements by use of the cell separator. Scand J Thorac Cardiovasc Surg 1985;19:165–71.
12. Moran JM, Babka R, Silberman S, Pifarré R, Sullivan HJ. Role of the Haemonetics Cell Saver following cardiopulmonary bypass. Proceedings of the Haemonetics Research Seminar. 1977:8–11.
13. Bull BS, Bull MH. Enhancing the safety of intraoperative RBC salvage. J Trauma 1989;29:320–5.
14. Wright G. Blood cell trauma. In: Taylor KM, ed. Cardiopulmonary bypass—principles and management. Cambridge: Chapman & Hall Medical, 1986:249–76.
15. Rommelsheim K, Schebusch H, Orellano L, Schwidetzky F, Klehr U. PMN elastase in extracorporeal circulation methods. Anaesth Intensivther Notfallmed 1987;22:3–7.
16. Fritz H. Proteinase inhibitors in severe inflammatory processes (septic shock and experimental endotoxemia): biochemical, pathophysiological and therapeutic aspects. Pro-

tein degradation in health and disease (a Ciba Foundation Symposium). Amsterdam: Excerpta Medica, 1980, 75:351.
17. Westaby S. Aspects of biocompatibility in cardiopulmonary bypass. CRC 1987;3:193–233.
18. Craddick PR, Fehr J, Brigham KL. Complement and leucocyte-mediated pulmonary dysfunction in hemodialysis. N Engl J Med 1977;296:769–74.
19. Bohler J, Kramer P, Gotze O. Leucocyte counts and complement activation during pump-driven and arteriovenous hemofiltration. In: Kramer P, ed. Arteriovenous hemofiltration. Göttingen: Vandenhaek & Ruprecht, 1982:187.
20. Boldt J, Kling D, v Bormann B, Scheld HH, Hempelmann G. Extravascular lung water and hemofiltration during complicated cardiac surgery. Thorac Cardiovasc Surg 1987;35:161–5.

Notice From the American Board of Thoracic Surgery Regarding Recertification

In 1973, the American Board of Medical Specialties recommended to its 23 member boards that periodic recertification become an integral part of all national medical specialty certification programs. To date, 17 of the member boards participate in recertification. The American Board of Thoracic Surgery (ABTS) has always regarded as its primary purpose the protection of the public through the establishment and maintenance of standards for the specialty. With the constructive intent of maintaining and advancing the standards of practice of thoracic surgery in the United States, the ABTS concluded in 1974 that its Diplomates should be recertified. The first time-limited certificates of the ABTS were issued in 1976, so essentially it has been the past 14 years that recertification has been required. During this time frame, approximately 75% of Diplomates have pursued recertification. It is the feeling of the Recertification Committee and the ABTS that our mission is to achieve 100% participation in recertification.

At the last meeting of the ABTS, the data of a survey of Diplomates regarding recertification, conducted by the Board secretary, Dr James V. Maloney, Jr, were presented. One hundred eleven questionnaires were sent to Diplomates holding expired certificates. Of those who completed the questionnaire, which was approximately 25%, three quarters felt that they were too busy in their practice and personal matters to go through the process. Some Diplomates had not obtained the required 100 hours of continuing medical education to qualify for recertification, and a few were afraid that they may not do well in the process. Importantly, almost half of the responses revealed a *misunderstanding of the requirements* of the recertification process.

The Recertification Committee is writing to you now in the hope that misinterpretations noted in this survey could be dispelled through publication of the facts surrounding the recertification process. The Recertification Committee would like to clarify the following information:

1. One may submit one's 100 most recent operative cases, *or the total year's experience if fewer than 100 cases are done annually*. There is no specific number of cases that you must do in order to be recertified. Indeed, some who have applied and received recertification have retired from active practice.
2. The ABTS accepts *all* approved postgraduate (category I and II) medical education credits, ie, continuing medical education credits do not have to be in thoracic surgery.
3. Any Diplomate is allowed to apply for recertification starting within 3 years of the expiration of his or her 10-year certificate. Expiration of a certificate will *not* disqualify a candidate for readmission to the recertification process.
4. The recertification process is, indeed, an educational process. In place of a cognitive examination, candidates for recertification are required to complete both the thoracic and cardiac portions of the SESATS syllabus (Self-Education/Self Assessment in Thoracic Surgery). Thus, taking the exam is essentially a home-learning experience of the applicant.

The Recertification Committee feels that the recertification process for thoracic surgery is fair and reasonable. It does not require taking an oral or proctored examination or going to a specific distant site. The recertification process is not meant to be punitive or probing. Most who have completed the process describe this procedure as a good, educational experience. It is our intent to make it known to all of those eligible for recertification that it is an excellent learning experience and an opportunity to review knowledge that has been added to the field in the 10 years since their certification. It provides reassurance both to patients and governmental authority that the individual surgeon is maintaining his or her clinical competence.

Recertification Committee:

George J. Magovern, MD, Chairman
Gordon F. Murray, MD
Mortimer J. Buckley, MD

Pulmonary Hypertension and Polymorphonuclear Leukocyte Elastase After Esophageal Cancer Operations

Nobuhiro Sato, MD, Kouji Murakami, MD, Kaoru Ishida, MD, Kenichirou Ikeda, MD, and Kazuyoshi Saito, MD

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To evaluate the role of polymorphonuclear leukocyte (PMN) elastase in pulmonary impairment occurring after operation for esophageal cancer, 10 patients were randomized preoperatively into two equal groups. One group received a placebo infusion and the other, an infusion of the PMN elastase inhibitor ulinastatin. In the placebo group, the mean plasma PMN elastase level increased from 154 ± 23 μg/L preoperatively to 449 ± 56 μg/L at 6 hours postoperatively ($p < 0.01$), whereas the mean plasma fibronectin concentration decreased from 490 ± 70 μg/mL preoperatively to 265 ± 81 μg/mL on postoperative day 2 ($p < 0.01$). The mean pulmonary vascular resistance increased markedly from 151 ± 24 dynes · s · $\text{cm}^{-5} \cdot \text{m}^{-2}$ preoperatively to 284 ± 76 dynes · s · $\text{cm}^{-5} \cdot \text{m}^{-2}$ at 6 hours postoperatively ($p < 0.01$). In the group given ulinastatin, 150,000 units every 12 hours from the start of the operation, the mean PMN elastase value at 6 hours postoperatively was lower (275 ± 66 μg/L; $p < 0.01$) and the fibronectin level on postoperative days 1 and 2, higher ($p < 0.05$). A lower pulmonary vascular resistance was noted into day 2 ($p < 0.05$). Our results suggest that PMN elastase may participate in the development of postoperative pulmonary impairment.

(Ann Thorac Surg 1991;51:754–8)

Pulmonary dysfunction that accompanies a severe injury has been theorized to be related to increased activation of the circulating blood cells, and the products of these cells, such as protease and free radicals, are thought to be involved in the direct mechanism of a pulmonary injury [1–3]. In view of the great stress that occurs to the body during an operation for esophageal cancer, it is possible that interaction between the bioactive substances and postoperative hypoxemia occurs. This may create an environment for the onset of a pulmonary complication.

This study was initiated to examine the postoperative changes in polymorphonuclear leukocyte (PMN) elastase and its role in the pulmonary circulation after radical lymph node dissection for thoracic esophageal cancer.

Material and Methods

Ten patients, ranging in age from 52 to 68 years (mean age, 61 years), who had a thoracic esophageal cancer were treated by surgical intervention without prior immunochemotherapy or irradiation. Before operation, the following variables were assessed in each patient: lung volume, pulmonary mechanics, liver function, and nutritional state. All patients were confirmed to be free from any previous pulmonary disease or any other preoperative complication that might affect the results. Written informed consent was obtained from each patient before the start of our study.

Operative Procedure

The operative technique used, ie, our current technique [4, 5], is summarized here. The right pleural cavity was entered through a posterolateral incision in the fifth intercostal space. The radical procedure was commenced with a thorough dissection of the supradiaphragmatic nodes, the posterior mediastinal nodes, the paraesophageal nodes, the bilateral pulmonary hilar nodes, the right paratracheal nodes, some of the left paratracheal nodes along the recurrent nerve, and the thoracic esophagus. These intrathoracic procedures were performed under one-lung anesthesia using an endotracheal tube.

After closure of the pleural cavity, the abdomen was entered through an upper midline incision, and the stomach was mobilized to create a gastric tube for the esophageal reconstruction. A proximal gastrectomy was performed with radical dissection of the lymph nodes along the common hepatic artery, the left gastric artery, the lesser curvature, and the cardia. A U-shaped incision was made in the neck, and then the cervical paraesophageal nodes, the right and left deep cervical nodes, and the supraclavicular nodes were radically dissected. For our reconstruction, the gastric tube was pulled up to the neck through the posterior mediastinum, and a gastroesophagotomy then followed.

Postoperative Evaluation

Lactated Ringer's solution was administered to maintain a pulmonary artery wedge pressure of 5 to 10 mm Hg from

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Table 1. Clinical Characteristics of the Patient Groups

	Ulinastatin Group (n = 5)			Placebo Group (n = 5)		
Variable	Mean	SD	Range	Mean	SD	Range
Age (y)	61	7	52–68	61	3	57–61
Operative time (h)	7.8	1.3	6.5–10	8.7	1.0	7.5–10
Fluid administered intraoperatively ($mL \cdot kg^{-1} \cdot h^{-1}$)	9.3	2.3	7.4–13.0	7.8	1.4	5.4–8.8
Estimated blood loss (mL)	704	273	420–1,110	738	201	550–1,030

SD = standard deviation.

the start of the operation until 6 AM on the first postoperative day. For nutritional support intravenous administration of glucose and amino acids, 30 to 40 calories $\cdot kg^{-1} \cdot 24\ h^{-1}$, was started beginning at 6 AM on postoperative day 1. No patient received any lipid infusion with the total parenteral nutrition during the study period.

At the end of the operation, all patients were immediately given prophylactic mechanical ventilation with a positive end-expiratory pressure of 5 cm H_2O in the intensive care unit. Fluid-filled catheters were used to measure the mean arterial pressure, the mean pulmonary artery pressure, and the pulmonary artery wedge pressure. Gas analysis of the arterial and the mixed venous blood was performed in the laboratories of the intensive care unit. The cardiac indices were measured by thermodilution with a thermistor-tipped pulmonary artery catheter. All measurements were obtained after each patient had been exposed to 100% oxygen at atmospheric pressure for 15 minutes.

The values reported were derived from the hemodynamic data and the blood gas analysis by the following equations [6, 7]:

$$\text{Pulmonary vascular resistance } (\text{dynes} \cdot s \cdot cm^{-5} \cdot m^{-2}) = 79.92 \times (MAP - PAWP)/CI.$$

$$\text{Intrapulmonary shunt rate (shunt flow/total flow)} = (CcO_2 - CaO_2)/(CcO_2 - C\bar{v}O_2) \times 100\%.$$

In the first equation, MAP = mean arterial pressure, PAWP = pulmonary artery wedge pressure, and CI = cardiac index. In the second equation, CaO_2 and $C\bar{v}O_2$ = oxygen content in arterial and pulmonary arterial blood, respectively, and CcO_2 = oxygen content in the capillary blood, derived from the alveolar gas equation, assuming a respiratory quotient of 1.

The PMN elastase that bound to the alpha$_1$-protease inhibitor was measured by an enzyme-linked immunoassay [8], and the plasma fibronectin concentration was determined by a single radial immunodiffusion assay using a partigen-fibronectin plate (Hoeschst-Behring Institute) [9].

The 10 patients were randomly divided into two groups of 5 each. One group received an intravenous infusion of ulinastatin (Mochida Pharmaceutical Co, Ltd, Tokyo, Japan), a protease inhibitor of inactivated PMN elastase. One unit of ulinastatin was defined as the amount inhibiting 2 μg of bovine pancreatic trypsin by 50%. The ulinastatin was given in a dose of 150,000 units every 12 hours from the start of the operation until the third postoperative day, with each dosage diluted in lactated Ringer's solution and infused for 3 hours. The other group of 5 patients received a placebo infusion in an identical manner.

The measurements for each patient were obtained 2 hours before and 6 hours after operation, and all subsequent measurements were done daily until postoperative day 5.

Statistical Analysis

All data are presented as the mean ± the standard deviation. The data were subjected to paired and nonpaired *t* tests, and a p value of less than 0.05 was considered significant.

Results

The postoperative course of each patient was satisfactory, and there were no hospital deaths. Further, there were no idiosyncratic reactions during the ulinastatin infusions.

The clinical characteristics of each group are given in Table 1. There was no appreciable difference between the two groups in age, operative time, amount of fluid administered, and volume of blood transfused. Blood transfusions, which seemed to influence the measurement of elastase and fibronectin, were administered only during the operation. Also, no patient was treated with a colloid infusion during the study period. Postoperative changes in pulmonary artery wedge pressure and cardiac index did not differ significantly between the groups; consequently, it was thought that the two groups reflected similar systemic hemodynamics.

In the placebo group, the operation resulted in an increase in PMN elastase from a preoperative level of 154 ± 23 μg/L to 449 ± 56 μg/L at 6 hours postoperatively ($p < 0.01$). Although the level gradually decreased, a significant elevation ($p < 0.05$) persisted up to postoperative day 5 (Fig 1). In contrast, the postoperative plasma fibronectin value decreased progressively from 490 ± 70 μg/L before operation to 265 ± 81 μg/mL on postoperative day 2 ($p < 0.01$) (Fig 2). The pulmonary vascular resistance rose from a preoperative value of 151 ± 24 dynes · s · $cm^{-5} \cdot m^{-2}$ to 284 ± 76 dynes · s · $cm^{-5} \cdot m^{-2}$ at 6 hours postoperatively ($p < 0.01$), and a significant increase ($p < 0.05$) was demonstrated up to day 3 (Fig 3). The pulmonary artery wedge pressure was maintained at 5 to 10 mm Hg, and the cardiac index remained unchanged, keeping its preoperative value of 3.57 ± 0.4 L · $min^{-1} \cdot m^{-2}$ during the study period. Finally, the intrapulmonary shunt rate increased significantly immediately postoperatively and remained elevated up to the end of day 5, reaching a maximum value of 23.5% ± 5.4% on day 2 ($p < 0.01$) (Fig 4).

In the ulinastatin group, PMN elastase also was elevated significantly, though the administration of ulinastatin kept the value lower (275 ± 66 μg/L at 6 hours postoperatively) than that in the placebo group ($p < 0.05$) (see Fig 1). There was no significant decrease in the concentration of fibronectin, which had a higher value than that of the placebo group from postoperative day 1 to postoperative day 2 ($p < 0.05$) (see Fig 2). A small increase in the pulmonary vascular resistance was noted from 142 ± 19 dynes · s · $cm^{-5} \cdot m^{-2}$ preoperatively to 173 ± 65 dynes · s · $cm^{-5} \cdot m^{-2}$ at 6 hours postoperatively. The values measured up to postoperative day 2 were significantly lower than those in the placebo group ($p < 0.05$) (see Fig 3). Finally, the marked increase in the intrapulmonary shunt rate was similar to that seen in the placebo group; it peaked at 21.8% ± 2.9% on postoperative day 2 (see Fig 4).

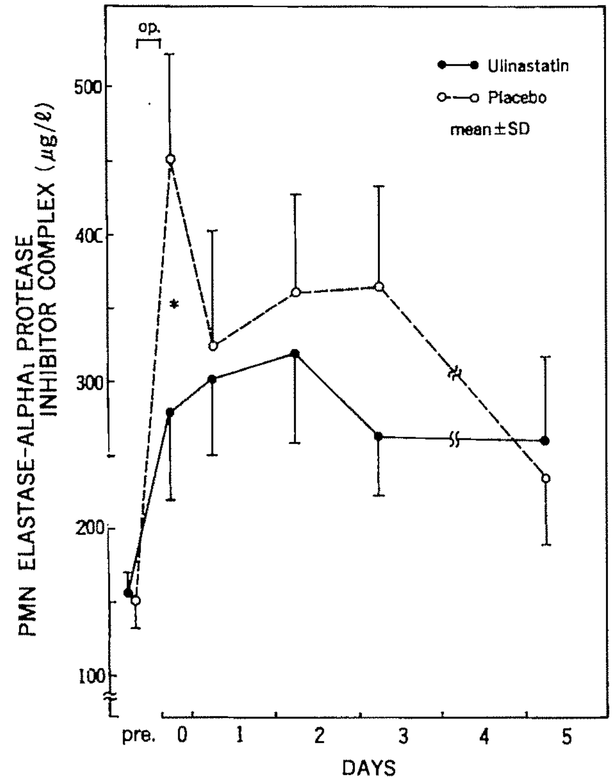

Fig 1. *Operation (op.) led to an increase in plasma polymorphonuclear leukocyte (PMN) elastase levels. The elevation was most prominent at 6 hours postoperatively, but significant increases were seen until day 5. Administration of ulinastatin resulted in a lower PMN elastase value. (SD = standard deviation; * = significant difference between placebo and ulinastatin groups.)*

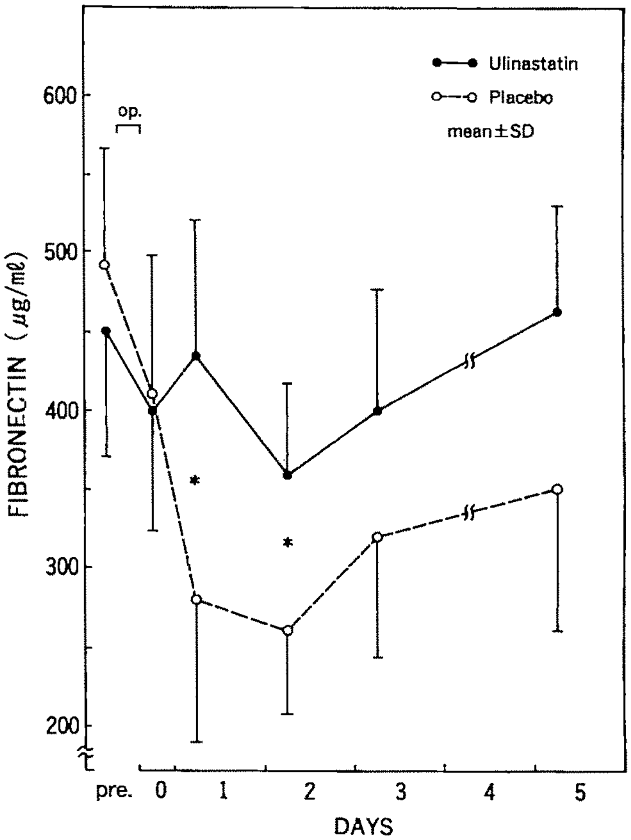

Fig 2. *Plasma fibronectin concentration decreased in the placebo group in contrast to the ulinastatin group. (op. = operation; SD = standard deviation; * = significant difference between placebo and ulinastatin groups.)*

There were no differences between the two groups in changes in the white blood cell count postoperatively.

Comment

Polymorphonuclear leukocyte elastase is known to display numerous bioactivities, such as the capability to degrade fibronectin, collagen, the proteoglycans, the basement membranes, and the surfactant apoproteins; it also can activate the complements and the clotting systems [10]. Further, elastase-induced damage to the endothelium and the basement membranes can alter the alveolar-capillary membrane permeability. In this regard, a previous study [11] has indicated that a trypsin inhibitor in a human urine preparation, ulinastatin, suppresses the activity of trypsin, PMN elastase, cathepsin G, and hyaluronidase, all of which participate in decomposing the extracellular and intracellular matrix. In Japan, this protective effect of ulinastatin on tissue degradation has been used for the treatment of acute pancreatic inflammation and shock [12]. More recently, ulinastatin has been spec-

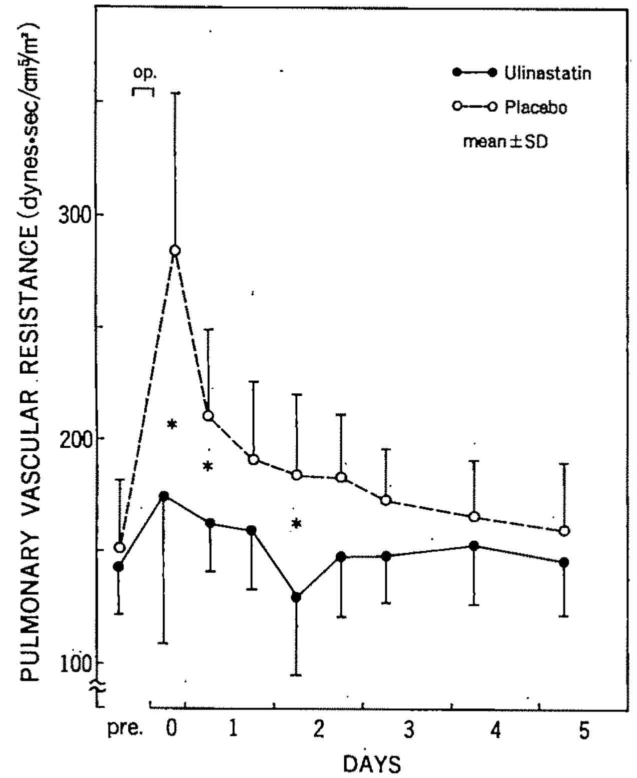

Fig 3. Operation (op.) *led to an increase in pulmonary vascular resistance in the placebo group. This increase was blunted by administration of ulinastatin.* (SD = *standard deviation;* * = *significant difference between placebo and ulinastatin groups.)*

ulated to possess potential benefits for treating acute pulmonary impairment.

After our total thoracic esophagectomy, which includes radical dissection of the lymph nodes, the plasma PMN elastase levels showed the most prominent increase at 6 hours postoperatively. Associated with the increase in PMN elastase were an increase in the pulmonary vascular resistance and a decrease in the concentration of plasma fibronectin, which cleared slowly over the next 2 days. That the inhibition of PMN elastase significantly limited pulmonary hypertension and the degradation of fibronectin suggests that PMN elastase somehow participates in the body's response to a pulmonary microvascular injury. The precise mechanism of how this is accomplished in this setting is unknown, though these results seem to indicate that PMN elastase directly influences the endothelial cell gap junctions by affecting the fibronectin content, opening the interendothelial junctions, and increasing the microvascular permeability.

Although pulmonary hypertension and degradation of fibronectin may be important in the development of pulmonary dysfunction, no significant difference was seen in the intrapulmonary shunt rate between the placebo and ulinastatin groups. The precise pathophysiology of an alveolar-capillary membrane injury is not yet clear. One hypothesis is the activation of the complements, the arachidonate metabolites, the cytokines, and the oxygen free radicals [13–15], though it remains questionable whether any of these mechanisms is more predominant. We cannot rule out such participation in the pathogenesis of a pulmonary injury. What can be proven, however, is that the pulmonary injury would have worsened.

Under certain conditions, PMN elastase plays a major role in a pulmonary injury. This can occur when a great amount of elastase develops, caused by a massive blood transfusion; or when the alpha$_1$-protease inhibitor is restrained by the development of a free radical, caused by tissue anoxia resulting from hypovolemia; or at the time of reexpansion because of improper inducement of one-lung anesthesia.

Other factors also must be considered. A broad spectrum of pulmonary impairments can occur after operation for esophageal cancer [16], and it is impossible to elucidate the status of postoperative hypoxemia only by noting the increase in PMN elastase levels and the decrease in fibronectin concentrations. Thorough dissection of the upper mediastinal lymph nodes constitutes a direct invasive assault on the respiratory system, thus causing injurious effects on the vagus nerve and the lymphatic vessels. These effects can lead to an increased microvascular permeability, and the excess fluids that accumulate may exceed the pumping ability of the lymphatic vessels [17].

Such conditions can be considered a preliminary stage of adult respiratory distress syndrome and should be viewed with concern, as even a slight incident can lead to a fatal complication. Thus, postoperative management should include preventive treatment for all possible

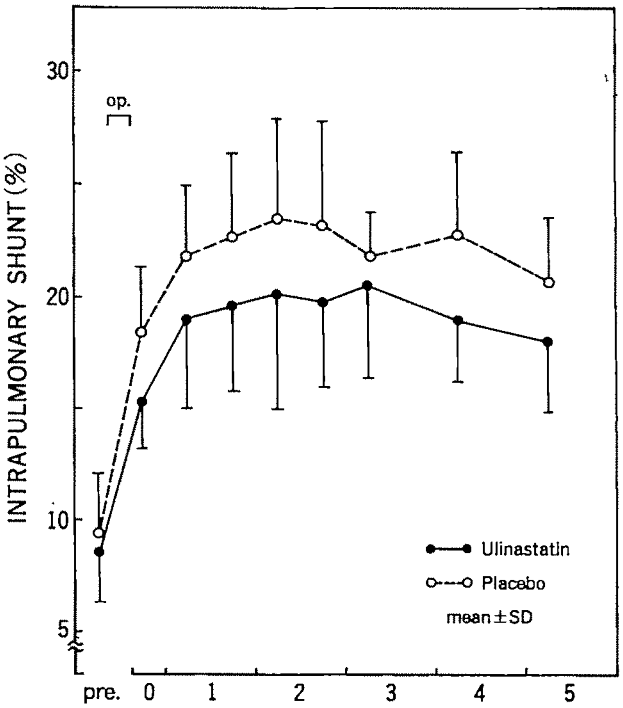

Fig 4. Operation (op.) *caused an increase in intrapulmonary shunt in both groups of patients.* (SD = *standard deviation.)*

pathological situations, and it is important to create as beneficial a milieu as possible for repair. Careful attention must be paid to various aberrant reactions that may be caused by bioactive substances.

In general, we did not observe any differences in clinical changes between the two groups even when PMN elastase was inhibited.

Our results suggest that under certain conditions, PMN elastase somehow participates in the postoperative mechanisms of a pulmonary injury within the pulmonary vasculature and causes a worsening of the condition, whereas other co-mediators and inhibitors may potentiate or neutralize each other. These mechanisms of intervention, acting at different stages in the pathogenesis of an injury, should be studied further in patients undergoing radical dissection of the upper mediastinal lymph nodes for thoracic esophageal cancer.

References

1. Malech HL, Gallin JI. Neutrophils in human diseases. N Engl J Med 1987;317:687–94.
2. Weiland JE, Davis WB, Holter JF, Mohammed JR, Dorinsky PM, Gadek JE. Lung neutrophils in the adult respiratory distress syndrome: clinical and pathophysiologic significance. Am Rev Respir Dis 1986;133:218–25.
3. Idell S, Kucich U, Fein A, et al. Neutrophil elastase-releasing factors in bronchoalveolar lavage from patients with adult respiratory distress syndrome. Am Rev Respir Dis 1985;132:1098–105.
4. Ishida K, Mori S, Okamoto K, et al. Results of extended dissection of lymph nodes in operation for thoracic esophageal cancer. In: Siewart IR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer-Verlag, 1987:690–2.
5. Akiyama H. Cardinals in the regional lymph node dissection in surgery of thoracic esophageal cancer. In: Siewart IR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer-Verlag, 1987:416–20.
6. Shoemaker WC. A new approach to physiology, monitoring, and therapy of shock states. World J Surg 1987;11:133–46.
7. Berggren SM. The oxygen deficit of arterial blood caused by non-ventilating parts of the lung. Acta Physiol Scand [Suppl] 1942;11:1–92.
8. Neumann S, Hennrich N, Gunzer G, Lang H. Enzyme-linked immunoassay for human granulocyte elastase in complex with alpha$_1$-proteinase inhibitor. In: Horl WH, Heidland A, eds. Protease. New York: Plenum, 1987:379.
9. Chadwick SJD, Mowbray JF, Dudby HAF. Plasma fibronectin and complement in surgical patients. Br J Surg 1984;71:718–20.
10. Havemann K, Gramse M. Physiology and pathophysiology of neutral proteinase of human granulocytes. In: Horl WH, Heidland A, eds. Protease. New York: Plenum, 1987:1.
11. Shibutani Y, Kunihiro Y. Preventative effects of ulinastatin on tissue degradation. Jpn Pharmacol Ther 1986;14:17–32.
12. Ohnishi H, Kosuzume H, Ashida Y, Kato K, Honjo I. Effect of urinary trypsin inhibitor on pancreatic enzymes and experimental acute pancreatitis. Dig Dis Sci 1984;29:26–32.
13. Kubo K, Kobayashi T. Effects of OK-046, a selective thromboxane-induced lung injury, in unanesthetized sheep. Am Rev Respir Dis 1985;132:494–9.
14. Bevilacqua MP, Pober JS, Wheeler ME, Cortran RS, Gimbrone MA. Interleukin-1 acts on cultured human vascular endothelium to increase the adhesion of polymorphonuclear leukocytes, monocytes, and related leukocyte cell lines. J Clin Invest 1985;76:2003–11.
15. Ratych RE, Chuknyiska RS, Bulkey GB. The primary localization of free radical generation after anoxia/reoxygenation in isolated endothelial cells. Surgery 1987;102:122–31.
16. Nakayama K, Kakegawa T. Latest management of pulmonary complications following esophageal cancer surgery in Japan. Int Adv Surg Oncol 1981;4:111–25.
17. Shimada I. The preserving effects of bronchial arteries and pulmonary nerves at radical esophagectomy on cardiorespiratory functions in the dog. Nippon Kyobu Geka Gakkai Zasshi 1989;37:2305–17.

Gastric Emptying After Gastric Interposition for Cancer of the Esophagus or Hypopharynx

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Transhiatal esophagectomy with primary anastomosis to the stomach (gastric pull-up) is an attractive surgical alternative to colic interposition in patients with cancer of the esophagus and hypopharynx. However, the lack of intrinsic gastric peristalsis and complaints by patients of postprandial regurgitation prompted us to measure the effect of body posture on the rates of gastric emptying in these patients. The rates of solid and liquid gastric emptying were measured in 14 patients who had undergone gastric interposition for esophageal and hypopharyngeal carcinoma. Rates of emptying were measured in both the supine and upright position using a dual-isotope radiolabeling technique. In these patients, the rate of gastric emptying of both solids and liquids was significantly slower in the supine position than in the upright position. Emptying in supine patients was also prolonged when compared with supine normal volunteers. Conversely, the upright rate of solid and liquid emptying in the patients was accelerated when compared with published values for upright normal volunteers. We conclude that gastric emptying after gastric interposition is dependent on upright posture after meals.

(Ann Thorac Surg 1991;51:759–63)

Despite recent advances in adjuvant therapy for esophageal and hypopharyngeal cancer, operation both for palliation and cure remains the most important hope for these patients [1–3]. Earlier surgical procedures were accompanied by unacceptably high rates of operative mortality and a degradation in the quality of life produced by techniques that precluded normal swallowing [4, 5]. In recent years, new surgical procedures have been developed that offer acceptably low mortality and complication rates, relieve obstruction, and restore the ability for normal or near-normal alimentation [6–9]. In one of the most popular of these techniques, the esophagus, with or without the hypopharynx, is resected and a primary anastomosis is created between the stomach and either the cervical esophagus, hypopharynx, or pharynx. This gastric interposition, or gastric pull-up, as it is sometimes called, can be accomplished through either a transhiatal or transthoracic approach and produces excellent functional results [10–14].

Although the technique of gastric interposition offers an improvement in nutrition and the quality of life by the preservation of swallowing, we have received frequent complaints of regurgitation after meals by patients having undergone this procedure. Because the stomach exhibits a lack of normal peristalsis when transposed to the chest, we speculated that emptying of the thoracic stomach may be dependent entirely on gravity. To test this hypothesis, we determined the rate of gastric emptying in both the supine and upright positions in a group of patients after gastric interposition for hypopharyngeal or esophageal carcinoma.

Material and Methods

Patient Selection

Fourteen patients were studied. Thirteen were male, 1 was female. The average age was 60 years (range, 43 to 83 years). Rates of gastric emptying were measured in all patients within an average of 3 months after gastric transposition (range, 1 to 16 months).

All patients underwent transhiatal gastric interposition (esophagectomy with primary anastomosis of the stomach to the proximal esophagus, pharynx, or hypopharynx) for carcinoma of the esophagus or hypopharynx. The interposed stomach was placed in the posterior mediastinum in the bed of the esophagus. Patients with carcinoma involving the cardia of the stomach were excluded from the series. All patients received a pyloroplasty at the time of operation. The proximal extent of esophageal resection differed in the group of patients: half of the 14 patients had pharyngolaryngoesophagectomies and half had esophagectomies.

The incidence of patients in this series reporting regurgitation after meals was 50% in this series. The symptom was more common in those patients who had pharyngolaryngoesophagectomies (5 of 7) than among those with esophagectomies (2 of 7).

Technique of Measuring Gastric Emptying

Eleven of the 14 patients underwent studies of gastric emptying in both supine and upright positions. Three underwent upright solid emptying studies only. All pa-

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tients were fed the radioactive meals while sitting. Consumption time for the meal was 10 minutes or less. Subsequently, those undergoing upright studies were standing for the actual imaging and sitting upright between images. Those undergoing supine studies were maintained continuously in the supine position after ingestion of the meal. When necessary for comfort, the patients were allowed to assume a lateral recumbent position for brief intervals during the supine study.

Patients were fed a 300-g meal consisting of dual-labeled solid and liquid phases. The solid phase was labeled with 600 μCi of technetium-99m (^{99m}Tc) sulfur colloid, which was injected into 20 to 50 g of liver pate and fried until crisp. This was then added to 150 g of thick canned beef stew. The liquid phase consisted of 150 mL of orange juice containing 100 μCi of indium 111 (^{111}In) DTPA. Imaging was performed according to a published protocol that uses correction for decay of radioactivity and corrects for attenuation by a technique that uses the geometric mean [15].

The efficacy and stability of radiolabeling and the validation of the technique of geometric mean have been previously reported [16–18]. The dose of exposure to radiation for the procedure is 0.11 mGy to the total body and 1.44 mGy to the stomach from ^{99m}Tc, and 0.24 mGy to the total body and 0.44 mGy to the stomach from ^{11}In [19].

Statistical Analysis

Statistical analysis of the data was performed using the software Stata (Computing Resource Center, Santa Monica, CA). Using this program, statistical significance between the supine and upright rates (equality of distributions) was calculated by the Wilcoxon sign-rank test.

Results

The tabulated data for the individual patients are shown in Table 1. Table 2 lists the statistical analysis of the data from Table 1. The rates of gastric emptying for both solids and liquids in this group of patients were significantly prolonged in the supine position when compared with the upright position ($p < 0.0033$). In Figure 1, this is illustrated by representative scintigraphic images of the solid phase of gastric emptying study in both the upright (upper panel) and supine (lower panel) positions.

Table 1. Patient Data

		$T_{1/2}$ (min)			
Patient No.	Type of Operation	Solid, Supine	Solid, Upright	Liquid, Supine	Liquid, Upright
1	PLE	158.7	9.1	68.8	9.6
2	PLE	95.5	80.5	67.3	34.9
3	PLE	3,000	7.8	3,000	7.9
4	EG	3,031	43	81	42
5	PLE	228.6	185.5	54.2	7.5
6	PLE	211.6	26.1	76.8	26.8
7	PLE	. . .	10	. . .	22
8	EG	2,400	45	1,300	44
9	EG	1,126	29	112	26
10	EG	371	30	243	20
11	EG	2,396	32	1,297	33
12	PLE	. . .	6.2	. . .	7.3
13	EG	. . .	5.5	. . .	5.9
14	EG	294	8	65	7

EG = esophagectomy; PLE = pharyngolaryngoesophagectomy; $T_{1/2}$ = time for emptying of one half of contents.

Although normal volunteers also exhibit a faster rate of gastric emptying in the upright than in the supine position [20], the positional discrepancy is even greater in patients after gastric interposition (see Table 2). In our patients, the rate of gastric emptying of both solids and liquids in the upright position was significantly increased when compared with published values for normal volunteers in the upright position ($p < 0.05$) [20, 21]. Conversely, the rate of solid emptying in the supine position was significantly prolonged ($p < 0.05$) when compared with supine normal volunteers [20]. (No normal values are available for emptying of liquids in the supine position.)

Because of differences in the proximal extent of tumor, half of the patients in this series had esophagectomies and half had pharyngolaryngoesophagectomies. However, no significant difference was seen in the rates of gastric

Table 2. Summary and Analysis of Patient Data[a]

Variable	Solid, Supine	Solid, Upright	Liquid, Supine	Liquid, Upright
Mean, normal[b]	116.9 (13.7)	75.7 (5.7)	. . .[c]	39.6 (4.8)
Mean, patients[b]	1,210.2 (371.7)	24.3 (5.73)	578.6 (282.7)	21 (3.7)
Standard deviation, patients	1,232.9	21.4	937.5	13.7
Minimum, patients	95.5	5.5	54.2	5.9
Maximum, patients	3,031	80.5	3,000	44

[a] Wilcoxon signed-ranks test (equality of distributions): (1) supine, liquid versus upright, liquid: probability > [Z], 0.0033; Z statistic, 2.93; (2) supine, solid versus upright, solid: probability > [Z], 0.0033; Z statistic, 2.93. [b] Numbers in parentheses are standard error of the mean. [c] Normal values not available.

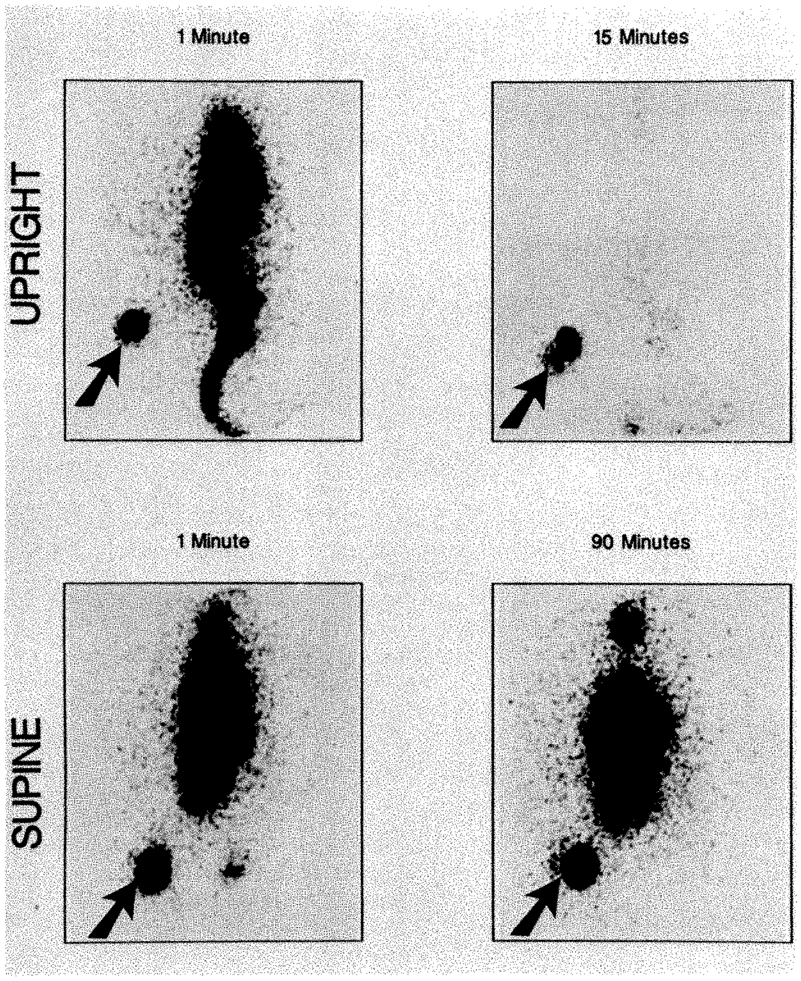

Fig 1. (Upper panel) Upright gastric emptying (anterior projection). Technetium 99m scintillation images of the anterior chest in a patient with gastric interposition (gastric pull-up). The patient maintained an upright posture after eating a radiolabeled meal. The image at left was taken 1 minute after completion of the meal and the image at right, 15 minutes after eating. The time for half the contents to empty ($T_{1/2}$) was 7.8 minutes for solids and 7.9 minutes for liquids. The arrow *points to a radioactive marker placed on the patient's skin to aid in positioning. (Lower panel) Supine gastric emptying (anterior projection). Technetium 99m scintillation images of the anterior chest in the same patient as in the upper panel. The patient maintained the supine position after eating a radiolabeled meal. The image at left was taken at 1 minute after, and the image at right 90 minutes after, the meal was eaten. Both solid and liquid $T_{1/2}$s were 3,000 minutes. The* arrow *points to a radioactive marker placed on the patient's skin to aid in positioning.*

emptying between these two groups ($p > 0.05$) in either the supine or upright position.

Comment

The management of esophageal carcinoma is controversial. Long-term survival is poor, despite recent advances in adjuvant therapy. Surgical management remains the basis of treatment of these patients, both with respect to prolongation of life and the quality thereof [1–3, 7, 9].

The surgical management of esophageal carcinoma is also controversial. Traditionally high rates of surgical mortality and complications have prompted some to advocate reserving resection only for those in whom a chance for cure exists [4, 5]. Recently, palliative surgical procedures have been developed that offer the opportunity for relief of obstruction, near-normal swallowing, and low rates of surgical mortality and complications [6–14]. In these surgical procedures, the esophagus (and, in certain patients, the hypopharynx or larynx as well) is resected and anastomosed either to the stomach or to a segment of colon or small bowel, which is interposed between the cervical alimentary tract and the stomach.

Gastric interposition is a particularly attractive approach to the surgical management of cancer of the esophagus. The stomach has an abundant blood supply and a long reach, and it is technically easy to use when compared with techniques of interposition of bowel. Patients usually receive a pyloroplasty at the time of operation to facilitate gastric emptying. The surgical approach can be either transthoracic (usually through the right hemithorax) or transhiatal [10–14]. The transhiatal approach offers a similar rate of operative complications to the transthoracic method and has the advantage of being useful in extending the indications for operation to patients at high surgical risk from a rib-spreading thoracotomy, such as patients with lung disease.

Nonetheless, there is a theoretical drawback to the technique of gastric interposition: the stomach does not retain peristalsis when transplanted to the chest. This feature, combined with three other factors, caused us to suspect that gastric emptying after gastric interposition is dependent on gravity and thus on the upright position. First, complaints by our patients of bothersome postprandial regurgitation were common (50% overall), especially in patients with pharygolaryngoesophagectomies. Second, there is extensive published experience that many factors can significantly affect the rate of gastric emptying, including body position [18, 20, 21]. Third, patients with esophageal cancer are often moribund, tire easily, and remain recumbent much of the time.

The results of this study support our hypothesis. When compared with published normal values [20], the rate of gastric emptying in patients after gastric interposition are markedly prolonged for both solids and liquids when the patient remains supine after ingesting the meal. In contrast, when a patient remains upright after eating (either sitting, standing, or a combination of the two), the rate of gastric emptying is actually accelerated when compared with normal values [20, 21]. The data strongly suggest a mechanism for the abnormality of gastric emptying in patients with gastric interposition. The rate of gastric emptying in the supine position is prolonged for both solids and liquids. This pattern has been observed in gastroparesis, such as that which can occur in diabetes [22]. In contrast, delayed gastric emptying due to a mechanical obstruction will typically demonstrate a markedly prolonged rate of solid emptying but a normal or near-normal rate of liquid emptying [23]. This pattern of delayed emptying seen in mechanical obstruction was not observed in our series. In fact, 1 patient who demonstrated markedly prolonged gastric emptying in the supine, but not upright, position underwent a second pyloroplasty. After the procedure, no change was observed in the rates of emptying in either the supine or upright position.

Half of our 14 patients had esophagectomies and half had hypopharyngolaryngoesophagectomies. There was no significant difference in the pattern of gastric emptying between the two groups. However, complaints of regurgitation were more common among those patients in whom both the hypopharynx and esophagus were resected (71%) than among those in whom only the esophagus (29%) was resected. In other words, sparing of the hypopharynx had no effect on the rate of emptying of the thoracic stomach but did correlate with fewer symptoms of regurgitation. This is further supported in the series of Orringer and Stirling [24], who reported excellent functional results after cervical esophagogastric anastomosis, with sparing of the hypopharynx, for benign disease.

In summary, we have found the procedure of transhiatal gastric interposition to be tolerated well. However, the rate of gastric emptying after the procedure is highly dependent on the patient maintaining an upright posture (either sitting, standing, or in combination) after meals. Whereas both solid and liquid rates of emptying are markedly prolonged in the supine position, they are either normal or accelerated in the upright position. The average time to empty one half of the stomach contents for solids in the upright position was 24 minutes. Therefore, if the patient were to remain upright for 1 hour after meals (approximately three half-lives), the thoracic stomach would essentially be emptied. Additionally, we have found that the dual liquid- and solid-phase isotopic method of determining gastric emptying is useful in evaluating problems related to swallowing in patients with gastric interposition.

References

1. Henessy TPJ. Choice of treatment in carcinoma of the oesophagus. Br J Surg 1988;75:193–4.
2. Mansour KA, Downey RS. Esophageal carcinoma: surgery without preoperative adjuvant chemotherapy. Ann Thorac Surg 1989;48:201–5.
3. Newaishy GA, Read GA, Duncan W, et al. Results of radical radiotherapy of squamous cell carcinoma of the oesophagus. Clin Radiol 1982;33:347–52.
4. Guili R, Gignoux M. Treatment of carcinoma of the oesophagus. Retrospective study of 2,400 patients. Am Surg 1980; 192:44–52.
5. Adelstein DJ, Forman SB, Beavers B. Esophageal carcinoma: a six year review of the Cleveland Veterans Administration Hospital experience. Cancer 1984;54:918–23.
6. LeQuesne LP, Ranger D. Pharyngolaryngectomy, with immediate pharyngogastric anastamosis. Br J Surg 1966;53: 105–9.
7. Schechter GL, Baker JW, Gilbert DA. Functional evaluation of pharyngoesophageal reconstructive techniques. Arch Otolaryngol Head Surg 1987;113:40–4.
8. Harrison DF. Surgical management of hypopharyngeal cancer. Arch Otolaryngol 1979;105:149–52.
9. Sugimachi K, Maekawa S, Koga Y, Ueo H, Inokuchi K. The quality of life is sustained after operation for carcinoma of the esophagus. Surg Gynecol Obstet 1983;162:544–6.
10. Stewart J, Sarr MG, Sharp KW, Efron G, Juanteguy J, Gadacz TR. Transhiatal esophagectomy for malignant and benign esophageal disease: clinical experience and technique. Ann Thorac Surg 1985;40:343–9.
11. Mathisen DJ, Grillo HC, Wilkins EW, Moncure AC, Hilgenberg AD. Transthoracic esophagectomy: a safe approach to carcinoma of the esophagus. Ann Thorac Surg 1988;45: 137–43.
12. Hankins JR, Attar S, Coughlin TR, et al. Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg 1989;47:700–5.
13. Orringer MB. Transthoracic esophagectomy without thoracotomy for carcinoma of the thoracic esophagus. Ann Surg 1984;200:282–8.
14. Goldberg M, Freeman J, Gullane PJ, Patterson GA, Todd TRJ, McShane D. Transhiatal esophagectomy with gastric transposition for pharyngolaryngeal malignant disease. J Thorac Cardiovasc Surg 1989;97:327–33.
15. Christian PE, Datz FL, Moore JG. Technical considerations in radionuclide gastric emptying studies. J Nucl Med Technol 1987;15:200–7.
16. Christian PE, Moore JG, Datz FL. In vitro comparison of solid food radiotracers for gastric emptying studies. J Nucl Med Technol 1981;9:116–7.
17. Heading RC, Tothill P, McLoughlin GP, et al. Gastric emptying rate measurement in man. A double isotope scanning technique for simultaneous study of liquid and solid components of a meal. Gastroenterology 1976;71:45–50.
18. Christian PE, Moore JG, Sorenson JA, et al. Effects of meal size and correction technique on gastric emptying time: studies with two tracers and opposed detectors. J Nucl Med 1980;21:883–5.
19. Siegel JA, Wu RK, Knight LC, et al. Radiation dose estimates for oral agents used in upper gastrointestinal diseases. J Nucl Med 1983;24:835–7.
20. Moore JG, Datz FL, Christian PE, Greenberg E, Alazraki N. Effect of body posture on radionuclide measurements of gastric emptying. Dig Dis Sci 1988;33:1592–5.
21. Moore JG, Christian PE, Coleman RE. Gastric emptying of

varying meal weight and composition in man. Evaluation by dual liquid and solid-phase isotopic method. Dig Dis Sci 1981;1:16–22.
22. Fox S, Behar J. Pathogenesis of diabetic gastroparesis (a pharmacologic study). Gastroenterology 1980;78:757–63.
23. Dubois A, Castell DO, eds. Esophageal and gastric emptying. Boca Raton, FL: CRC Press, 1984.
24. Orringer MB, Stirling MC. Cervical esophagogastric anastomosis for benign disease—functional results. J Thorac Cardiovasc Surg 1988;96:887–93.

REVIEW OF RECENT BOOKS

Anesthesia for Cardiac Surgery
By James A. DiNardo and Michael J. Schwartz
Norwalk, CT, Appleton & Lange, 1990

Reviewed by Ellen L. Finch, MD

The authors of *Anesthesia for Cardiac Surgery,* Drs James DiNardo and Michael Schwartz, set out to write a concise yet comprehensive textbook for anesthesiologists training in cardiac anesthesia. They have been remarkably successful in accomplishing this stated goal, and have filled a need recognized by many of those teaching residents and fellows in the field. Cardiac anesthesiologists today are expected to be knowledgeable about a broad range of technical procedures specific to cardiac surgery, as well as about the special problems of the cardiac patient. As a result, the numbers of anesthesiologists seeking specialized training in this field are growing. Although a number of textbooks on cardiac anesthesia have been published in recent years, from outline-style manuals to lengthy reference volumes on cardiac physiology and pharmacology, previously it has been difficult to identify one single book as an appropriate primary text for the cardiac anesthesiologist in training. With the publication of *Anesthsia for Cardiac Surgery,* such a recommendation can be made with confidence.

Drs DiNardo and Schwartz, as well as each of the four other contributing authors, received their training in cardiac anesthesia at the Beth Israel Hospital of the Harvard Medical School. This allows for an overall consistency in philosophy and technique uncommon in a multiauthor text. Each chapter is divided into discussion of physiology and of anesthetic considerations. Chapter-to-chapter duplication of material is minimal. The complexity of the discussion is appropriate for the relatively experienced anesthesiologist who does not routinely care for cardiac surgical patients. Specific anesthetic plan recommendations are presented in a useful way. References throughout are ample and recent.

The book includes chapters on preoperative assessment, interpretation of cardiac catheterization data, monitoring, cardiopulmonary bypass, myocardial preservation, central nervous system injury, and postoperative care as well as individual chapters on each of the major types of cardiac surgery. Several sections are outstanding. The chapter on "Valvular Heart Disease" integrates pathophysiology with specific, well-defined anesthetic goals for each of the common valvar defects. The chapter on "Congenital Heart Disease" includes an excellent discussion of neonatal cardiac physiology and offers a useful review of the important anesthetic considerations for each of the most common congenital repairs. The "Central Nervous System Injury" chapter deals clearly with the complex and often misunderstood issues of temperature correction of blood gases, barbituate cerebral protection, and postoperative stroke.

The authors made an obvious effort to limit the length of the book to make it more practical to carry and less costly to purchase. Certain important subjects, however, have been entirely omitted. Heart and lung transplantation, intraoperative mapping and arrhythmia operations, and left ventricular assist device implantation are all routine procedures for many cardiac anesthesiologists. The decision not to include these subjects may reflect the surgical practice at the authors' institution, but it does result in a less comprehensive review of the full range of responsibilities of the cardiac anesthesiologist.

Although the experienced cardiac anesthesiologist will find many sections of this well-written, up-to-date book an excellent review, it is not most useful as a reference text. For example, there is only one sentence on management of partial (left heart) bypass, and no mention is made of anesthetic considerations in idiopathic hypertrophic subaortic stenosis. In contrast, anesthesia for the patient with valvar aortic stenosis is covered in great detail. Anesthesia for routine coronary artery surgery is discussed at length. This deliberate emphasis on "the basics" is both the strength and the limitation of this excellent book. It will be of most interest and value to anesthesiologists learning cardiac anesthesia, but will also be of interest to cardiac surgeons, medical students, and others interested in understanding what the cardiac anesthesiologist does. It belongs in the library of anesthesia residency training programs, and will undoubtedly become a popular addition to the personal libraries of the cardiac anesthesiologists of tomorrow.

San Diego, California

Erythropoietin Deficiency After Coronary Artery Bypass Procedures

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Erythropoietin is the primary regulator of erythropoiesis. Erythropoietin has been shown to increase exponentially in response to linear decreases in hematocrit in normal, unstressed animals. However, the effect of operation, with its attendant stress, on erythropoietin levels is unknown. The purpose of this study is to evaluate the effect of surgical stress on erythropoietin. Twenty otherwise healthy patients scheduled for elective surgical procedures were studied. The cholecystectomy group included 10 patients who underwent cholecystectomy for documented stone disease. Ten patients who underwent coronary artery bypass procedures constituted the coronary artery bypass grafting group. Patients were studied preoperatively as well as on the first and second postoperative days. The hematocrit and erythropoietin levels were similar in both groups preoperatively. The hematocrit in the coronary artery bypass grafting group was lower than that of the cholecystectomy group on postoperative day 1 (0.31 versus 0.36; $p < 0.003$) and postoperative day 2 (0.30 versus 0.36; $p < 0.001$). During the first two postoperative days the erythropoietin levels were similar between groups. The data show that postoperative erythropoietin levels are similar after coronary artery bypass grafting, despite more severe anemia, when compared with cholecystectomy. This suggests that after coronary artery bypass grafting there is a relative deficiency of erythropoietin. Administration of recombinant human erythropoietin to patients undergoing surgical procedures could correct the erythropoietin deficiency and accelerate postoperative erythropoiesis.

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Erythropoietin is the primary regulator of erythropoiesis during anemia [1]. Erythropoiesis has been reported to be decreased after surgical procedures [2]. Serum erythropoietin levels increase exponentially in response to linear decreases in hematocrit [3, 4]. Erythropoietin levels have been shown to be depressed in a variety of experimental [5, 6] and clinical [7–13] settings. However, the effect of operation and its attendant stress on erythropoietin levels is unknown. The purpose of this study is to evaluate the effect of operation on erythropoietin levels.

Material and Methods

This protocol was approved by the Institutional Review Board on Human Experimentation and all subjects gave written informed consent before participation. Patients were scheduled for elective surgical procedures and had no history of malignancy, steroid therapy, chemotherapy, radiotherapy, unexplained anemia, recent blood loss, renal disease, or urologic pathology. Further, to be included in the study, preoperative laboratory values for hemoglobin, hematocrit, red cell indices, platelet count, bilirubin, blood urea nitrogen (BUN), creatinine, and albumin all had to be within normal limits. Two groups of patients were studied. Ten patients undergoing cholecystectomy for documented stone disease comprised the CHTX group. Ten patients undergoing coronary artery bypass procedures comprised the CABG group.

For editorial comment, see page 703.

Patients had blood drawn for complete blood count, reticulocyte and platelet counts, and measurement of erythropoietin levels preoperatively and on postoperative days (PODs) 1, 2, and 4. Specimens were obtained from all patients for BUN and creatinine on POD-2. Albumin levels were determined preoperatively.

The complete blood count, reticulocyte and platelet counts, and BUN, creatinine, and albumin level determinations were all made by standard methods. Erythropoietin levels were determined by radioimmunoassay [14]. Comparisons were made using paired and unpaired Student's t tests as appropriate. Statistical significance was defined as a p value less than 0.05. Data are presented as mean ± standard error of the mean throughout this report.

Results

All patients survived the protocol and were discharged from the hospital alive. Then mean age of the CABG group was significantly greater than that of the CHTX group (64 ± 3 versus 47 ± 5 years; $p < 0.01$). The CABG group received 3.4 ± 0.7 units of packed red blood cell transfusions perioperatively. No patient in the CHTX

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Table 1. Hematocrit

Group	Preoperative	POD 1	POD 2	POD 4
CHTX	0.39 ± 0.01	0.36 ± 0.01	0.36 ± 0.01	0.34 ± 0.01
CABG	0.40 ± 0.01	0.31 ± 0.01	0.30 ± 0.01	0.35 ± 0.01
p Value	NS	0.003	0.001	NS

CABG = coronary artery bypass grafting; CHTX = cholecystectomy; NS = not significant; POD = postoperative day.

group received a transfusion. There were no significant differences between groups in preoperative values of albumin, hemoglobin, hematocrit, erythropoietin level, and reticulocyte count. Preoperative values for bilirubin, BUN, and creatinine were all within the normal range. The CABG group had higher levels of BUN (5.7 ± 0.4 versus 7.3 ± 0.6 mmol/L of urea; $p < 0.011$) and creatinine (97 ± 9 versus 80 ± 9 μmol/L; $p < 0.04$). The CHTX group had 10 female patients as opposed to 3 in the CABG group.

The CABG group had an average of three bypass grafts accomplished with a mean aortic cross-clamp time of 52 ± 4 minutes and 118 ± 10 minutes of extracorporeal circulation using a membrane oxygenator. Six patients in the CABG group had internal mammary artery to coronary artery anastomoses, and 2 required postoperative support with intraaortic balloon pumps. All patients in this group were extubated on POD 1. There were no infections or complications in this group. Three patients in the CHTX group underwent common bile duct exploration, 1 of these underwent a choledochoduodenostomy, and 1 patient in the CHTX group had a wound infection diagnosed on POD 6.

The hematocrits are shown in Table 1. Both groups had similar hematocrits preoperatively. On PODs 1 and 2 the hematocrits were significantly lower in the CABG group. Both groups had significant decreases in hematocrit postoperatively when compared with preoperative values. The groups had similar hematocrits on POD 4.

The erythropoietin levels are shown in Table 2. The erythropoietin levels were similar between groups preoperatively and on PODs 1, 2, and 4. The erythropoietin levels remained significantly elevated postoperatively ($p < 0.05$ on PODs 1, 2, and 4) in the CHTX group as compared with the preoperative values. The erythropoietin levels in the CABG group remained similar to preoperative values throughout the postoperative period.

There were no significant differences between groups in white blood cell counts preoperatively or postoperatively. The platelet and reticulocyte counts are shown in Table 3. The reticulocyte counts were similar between groups throughout the study. Platelet counts were higher in the CHTX group throughout the study. There were no differences between groups in postoperative (POD 2) levels of BUN or creatinine.

Comment

Erythropoietin is the primary regulator of erythropoiesis during anemia. Erythropoietin has been shown to increase exponentially in response to linear decreases in hematocrit in normal, unstressed animals [3, 4]. Deficiency of erythropoietin results in decreased erythropoiesis in a variety of clinical and experimental settings [5–13]. Decreased erythropoiesis has been reported after surgical procedures [2]. The effect of operation on erythropoietin is unknown and is the focus of this report.

Patients undergoing CABG were more anemic in the early postoperative period (PODs 1 and 2) than patients undergoing CHTX. More serious levels of anemia should have been associated with significant elevations of erythropoietin levels [3, 4, 14–17]. However, the erythropoietin levels were similar between groups during this time period, suggesting an erythropoietin-deficient state in the early postoperative period after CABG.

The groups in this study differed significantly in several respects. The CHTX group was significantly younger and entirely female; however, age and sex have been shown not to be significant determinants of erythropoietin levels [17]. Although both groups underwent major operative procedures under general anesthesia, coronary artery bypass procedures are associated with greater stresses and more intensive pharmacological and ventilatory support than cholecystectomy patients. The role of these factors is unclear. Only patients in the CABG group received transfusions and underwent extracorporeal circulation. The effects of transfusion per se and extracorporeal perfusion on erythropoietin production are unknown.

Preoperative values for BUN and creatinine, although within the normal ranges, were both higher in the CABG group. Because the kidney is the primary site of erythropoietin production [18] it is likely that this difference in renal function is a contributing factor in the difference between groups. However, the difference in renal function between groups is unlikely to be the sole factor responsible for the erythropoietin deficiency in the CABG group. The combination of hypoperfusion during extracorporeal perfusion and slightly decreased baseline renal function may explain erythropoietin deficiency after CABG. The precise mechanism of erythropoietin deficiency will clearly require further investigation.

The erythropoietin levels seen in this study were too low to cause a meaningful reticulocytosis, despite the mild anemia. Endogenous erythropoietin levels of less than 500 mU/mL have been show to predict a good response to exogenous administration of erythropoietin [19]. The serum erythropoietin level necessary for maximal stimulation of erythropoiesis is unknown, but is likely to be much greater than 500 mU/mL [4, 10, 20, 21]. Therefore, the CABG group appears to have a relative

Table 2. Erythropoietin Levels (mU/mL)

Group	Preoperative	POD 1	POD 2	POD 4
CHTX	32.4 ± 3.7	58.4 ± 12.1	55.6 ± 7.8	48.3 ± 7.6
CABG	37.8 ± 4.7	38.9 ± 5.5	57.6 ± 10.3	43.2 ± 5.5
p Value	NS	NS	NS	NS

CABG = coronary artery bypass grafting; CHTX = cholecystectomy; NS = not significant; POD = postoperative day.

Table 3. Platelet and Reticulocyte Counts

	Preoperatively		POD 1		POD 2		POD 4	
Group	RTC	Plt	RTC	Plt	RTC	Plt	RTC	Plt
CHTX	1.8 ± 0.3	352 ± 19	2.2 ± 0.5	326	1.6 ± 0.4	309 ± 23	2.2 ± 0.6	478 ± 4
CABG	1.5 ± 0.2	271 ± 25	1.9 ± 0.4	122 ± 12	1.9 ± 0.3	104 ± 10	2.6 ± 0.3	165 ± 20
p Value	NS	0.021	NS	0.0001	NS	0.0001	NS	0.0001

CABG = coronary artery bypass grafting; CHTX = cholecystectomy; NS = not significant; Plt = platelet count (10^9/L); POD = postoperative day; RTC = reticulocyte fraction (10^{-3}).

erythropoietin deficiency in the early postoperative period, and this deficiency could lead to substantial slowing of erythropoiesis.

The risks associated with homologous blood transfusion have forced a reassessment of transfusion practice [22, 23]. This has renewed interest in preoperative autologous donation and intraoperative red cell salvage techniques. Maximizing perioperative erythropoiesis is an additional alternative to the risks of homologous transfusion [20]. Recombinant erythropoietin administration increases erythropoiesis in a variety of erythropoietin-deficient states [19, 24, 25]. Administration of recombinant erythropoietin has been shown to increase erythropoiesis enough to significantly augment yields of preoperative autologous donation programs [26, 27], as well as accelerating regeneration of red cells in models of perioperative anemia [20, 21]. The presence of an erythropoietin-deficient state in the early postoperative period after CABG procedures may make perioperative erythropoietin administration particularly efficacious; however, confirmation of this hypothesis will clearly require data from a controlled clinical trial.

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References

1. Goldwasser E. Erythropoietin and the differentiation of red blood cells. Fed Proc 1975;34:2285–92.
2. Gould SA, Rosen AL, Sehgal LR, et al. Depressed red cell recovery following acute blood loss. Fed Proc 1985;44:1265.
3. Adamson JW. The erythropoietin/hematocrit relationship in normal and polcythermic man: implications of marrow regulation. Blood 1968;32:597–609.
4. Rosen AL, Gould SA, Sehgal LR, et al. Erythropoietic response to acute anemia. Crit Care Med 1990;18:298–302.
5. Lukens JN. Control of erythropoiesis in rats with adjuvant-induced chronic inflammation. Blood 1973;41:37–44.
6. Weiss DJ, Krehbiel JD, Lund JE. Studies of the pathogenesis of anemia of inflammation: mechanism of impaired erythropoiesis. Am J Vet Res 1983;44:1832–5.
7. Douglas SW, Adamson JW. The anemia of chronic disorders: studies of marrow regulation and iron metabolism. Blood 1975;45:55–65.
8. Ward HP, Kurnick JE, Pisarczyk MI. Serum level of erythropoietin in anemias associated with chronic infection, malignancy and primary hematopoietic disease. J Clin Invest 1971;50:332–5.
9. Zucker S, Friedman S, Lysik RM. Bone marrow erythropoiesis in the anemia of infection, inflammation and malignancy. J Clin Invest 1974;53:1132–8.
10. Sherwood JB, Goldwasser E, Chilcote R, et al. Sickle cell anemia patients have low erythropoietin levels for their degree of anemia. Blood 1986;67:46–9.
11. Robinson H, Monafo WW, Saver SM, Gallagher NI. The role of erythropoietin in the anemia of thermal injury. Ann Surg 1973;178:565–72.
12. Spivak JL, Barnes DC, Fuchs E, Quinn TC. Serum immunoreactive erythropoietin in HIV infected patients. JAMA 1989; 261:3104–7.
13. Christensen RD. Recombinant erythropoietic growth factors as an alternative to erythrocyte transfusion for patients with "anemia of prematurity." Pediatrics 1989;83:793–5.
14. Egrie JC, Cotes PM, Lane J, et al. Development of radioimmunoassays for human erythropoietin using recombinant erythropoietin as tracer and immunogen. J Immunol Methods 1987;99:235–41.
15. Erslev AJ, Wilson J, Caro J. Erythropoietin titers in anemic, nonuremic patients. J Lab Clin Med 1987;109:428–33.
16. Miller ME, Cronkite EP, Garcia JF. Plasma levels of immunoreactive erythropoietin after acute blood loss in man. Br J Hematol 1982;52:545–9.
17. Miller ME, Chandra M, Garcia JF. Clinical applications of measurement of serum immunoreactive levels of erythropoietin. Ann NY Acad Sci 1985;459:375–81.
18. Erslev AJ, Caro J, Besarab A. Why the kidney? Nephron 1985;41:213–6.
19. Fischl M, Galpin JE, Levine JD, et al. Recombinant human erythropoietin for patients with AIDS treated with zidovudine. N Engl J Med 1990;322:1988–93.
20. Levine EA, Gould SA, Rosen AL, et al. Perioperative recombinant human erythropoietin. Surgery 1989;106:432–8.
21. Levine EA, Rosen AL, Sehgal LR, et al. Treatment of acute postoperative anemia with recombinant human erythropoietin. J Trauma 1989;29:1134–9.
22. Zuck TF. Transfusion-transmitted AIDS reassessed. N Engl J Med 1988;318:511–2.
23. Bove JR. Transfusion associated hepatitis and AIDS. N Engl J Med 1987;317:242–5.
24. Eschbach JW, Egrie JC, Downing MR, et al. Correction of the anemia of end stage renal disease with recombinant human erythropoietin. N Engl J Med 1987;316:73–8.
25. Winearls CG, Oliver DO, Pippord MJ, et al. Effect of human erythropoietin derived from recombinant DNA on the anemia of patients maintained by chronic hemodialysis. Lancet 1986;2:1775–8.
26. Goodnough CT, Rudnick S, Price JH, et al. Increased preoperative collection of autologous blood with recombinant human erythropoietin therapy. N Engl J Med 1989;321:1163–8.
27. Levine EA, Rosen AL, Gould SA, et al. Recombinant human erythropoietin and autologous blood donation. Surgery 1988; 104:365–9.

Autologous Blood Transfusion With Recombinant Human Erythropoietin in Heart Operations

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The effects of recombinant human erythropoietin (rHuEPO) on improving the anemia associated with autologous blood collection before open heart operations and on improving the postoperative anemia were studied. The study was carried out on 18 patients undergoing coronary artery bypass operations; 400 mL of autologous whole blood was taken from each patient 2 weeks before operation and was subsequently used in the operation, and rHuEPO (100 U · kg^{-1} · day^{-1}) was given intravenously for 2 weeks before operation and for 1 week after operation. The group in which iron preparations were also administered intravenously was designated as group I (10 patients), and the group in which rHuEPO was given alone was designated as group II (8 patients). In group III, as a control group, 11 past patients were used in whom 400 mL of autologous whole blood was collected 2 weeks before operation but neither rHuEPO nor iron preparations were given. After autologous blood collections, the hemoglobin levels improved in group I, group II, and group III, in that order, and with significant differences among them. It was shown that rHuEPO was effective in ameliorating the anemia associated with preoperative autologous blood collection, and the effect was further enhanced with intravenous supplementing iron preparations. After operation, the anemia markedly improved while rHuEPO was administered, but the hemoglobin levels decreased rapidly when the administration was terminated. Further studies are needed regarding the use of rHuEPO after operation.

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In our hospital, we have been collecting autologous blood before elective open heart operations since 1986 to minimize transfusion of homologous blood [1]. However, 3 to 4 weeks are usually necessary for recovery from anemia after collection of 400 mL of autologous whole blood and about 2 months are necessary before operation if 800 mL, the volume usually required to avoid the need for any homologous blood transfusion, is collected.

The present study evaluated the effects of recombinant human erythropoietin (rHuEPO) on autologous blood collection before open heart operations and on postoperative anemia.

For editorial comment, see page 703.

Material and Methods

Eighteen randomly chosen patients with stable angina who were waiting for coronary artery bypass operations were divided into two groups. In Group I (10 patients), 400 mL of autologous whole blood was collected before operation and was subsequently used in the operation. After the collection of autologous blood, rHuEPO (100 U · kg^{-1} · day^{-1}) was administered intravenously every day for 3 weeks, from 2 weeks before operation to 1 week after operation. Iron preparations were also administered: short-term preoperative iron supplementation was considered, and 40 mg of chondroitin sulfate-iron was given intravenously every day. In group II (8 patients), 400 mL of autologous whole blood was taken 2 weeks before operation, and rHuEPO was administered every day in the same manner as in group I, but no iron preparation was administered.

Eleven earlier patients who had undergone coronary artery bypass operations before rHuEPO was available were chosen as a control group (group III). In this control group, 400 mL of autologous whole blood was collected 2 weeks before operation, and thereafter neither rHuEPO nor iron preparation was administered. No homologous blood transfusion was required during and after operation as a result of the autologous transfusion.

These patients did not have such anamneses as hematological diseases, inflammatory diseases, infectious diseases, or neoplasms, which could affect the bone marrow response. They had no history of taking steroids or of alcohol abuse.

The observation period was from 2 weeks before operation to 3 weeks after operation; during that period the hemoglobin level, reticulocyte count, number of platelets,

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Table 1. Characteristics of the Three Groups[a]

Variable	Group I (N = 10)	Group II (N = 8)	Group III (N = 11)	*p* Value
Age (y)				
Mean ± SD	54.7 ± 6.9	56.9 ± 9.9	56.1 ± 10.5	NS
Minimum	41	45	38	
Maximum	65	68	73	
Sex				
Male	10	8	11	NS
Female	0	0	0	
Body weight (kg)	66.0 ± 8.6	62.2 ± 10.2	57.8 ± 5.0	NS
Hemoglobin (g/L)	136 ± 10	147 ± 11	147 ± 7	NS
Reticulocytes ($\times 10^9$/L)	65 ± 15	63 ± 34	57 ± 14	NS
ECC time (minutes)	183 ± 38	180 ± 22	148 ± 53	NS
Postop 24-h bleeding (mL)	391 ± 100	466 ± 79	460 ± 135	NS

[a] Where appropriate, data are shown as mean ± standard deviation.

ECC = extracorporeal circulation; NS = not significant; Postop 24-h bleeding = volume of blood drained during 24 hours after operation; SD = standard deviation.

number of white blood cells, and serum iron level were measured twice a week.

The use of rHuEPO was explained to the patients and written consent was obtained from each of them before the administration of rHuEPO.

For statistical analysis, the one-way layout variance analysis (Scheffé's method) was used to test the differences between the three groups [2]. Significance was set at the 5% confidence level.

Results

Table 1 shows the age, sex, body weight, hemoglobin level, and reticulocyte count before autologous blood donation, extracorporeal circulation time, and amount of drained blood for 24 hours after operation of each group. For each item there was no significant difference between the three groups.

Neither group I nor group II required homologous blood transfusion during or after operation.

Figure 1 shows the absolute hemoglobin levels of each group before and after operation. Hemoglobin levels immediately before operation were 148 ± 6, 145 ± 15, and 135 ± 8 g/L in groups I, II, and III, respectively. There were no significant differences among the three groups concerning these data, but the hemoglobin levels immediately before operation were greater in group I, almost equal in group II, and lower in group III, compared with the level before autologous blood donation. Hemoglobin levels on the first day after operation were 112 ± 7, 116 ± 17, and 104 ± 16 g/L in groups I, II, and III, respectively. There were no significant differences among the three groups. However, the hemoglobin levels in groups I and II increased thereafter, resulting in significant differences between groups II and III on days 4, 7, 10, and 14, and between groups II and III on days 7 and 10. The hemoglobin levels on day 21 were 117 ± 10, 121 ± 17, and 113 ± 8 g/L in groups I, II, and III, respectively, with no significant differences among the three groups.

The differences between hemoglobin levels before autologous blood donation and thereafter were shown as the degree of improvement in preoperative anemia after donation (Fig 2). In group I the preoperative change in hemoglobin level was +2 ± 9 g/L on the fourth day before operation; this was significantly different compared with group III. The preoperative change in hemoglobin level immediately before operation was +11 ± 8, −2 ± 6, and −12 ± 8 g/L in groups I, II, and III, respectively; there were significant differences between groups I and III ($p < 0.05$), groups II and III ($p < 0.05$), and groups I and III ($p < 0.01$).

The degree of improvement in postoperative anemia was evaluated based on the differences between hemoglobin levels determined the first day after operation and thereafter (Fig 3). On days 7, 14, and 21 after operation the postoperative change in hemoglobin level was +23 ± 10, +12 ± 13, and +5 ± 10 g/L in group I; +26 ± 11, +8 ± 11, and +6 ± 11 g/L in group II; and +7 ± 10, +6 ± 11, and +8 ± 14 in group III, respectively. In groups I and II increases in hemoglobin levels were statistically significant on day 7 compared with group III ($p < 0.05$ and $p < 0.01$). However, the hemoglobin levels decreased rapidly thereafter, resulting in no significant differences among the three groups on days 14 and 21.

Figure 4 shows the reticulocyte counts during the observation period. On days 14 and 7 and immediately before operation the reticulocyte counts were 64 ± 15, 225 ± 46, and 239 ± 34 × 10^9/L in group I; 63 ± 34, 157 ± 97, and 161 ± 70 × 10^9/L in group II; and 57 ± 14, 86 ± 9, and 84 ± 14 × 10^9/L in group III, respectively. Increases in reticulocyte counts were significant compared with group III in groups I and II starting on the seventh and fourth days before operation. On days 1, 7, 14, and 21 after operation the reticulocyte counts were 183 ± 37, 238 ± 51,

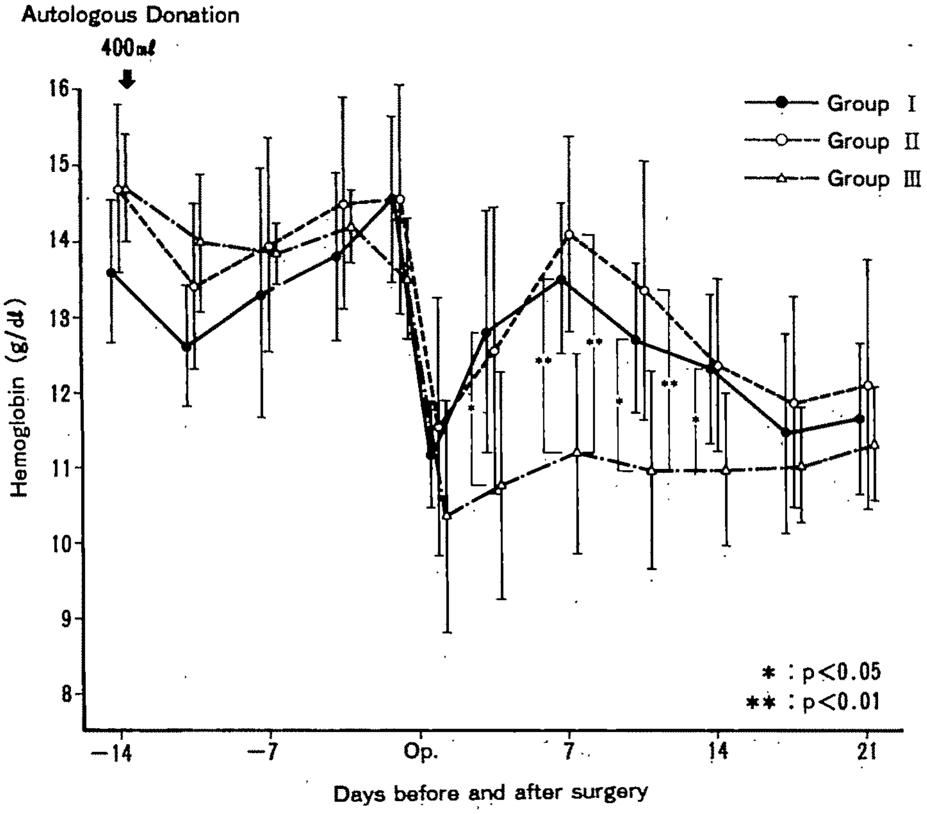

Fig 1. Changes in absolute hemoglobin levels before and after operation (Op. = the day of operation.)

65 ± 25, and 43 ± 11 × 10^9/L in group I; 170 ± 88, 217 ± 83, 55 ± 20, and 32 ± 20 × 10^9/L in group II; and 43 ± 16, 81 ± 36, 132 ± 79, and 80 ± 21 × 10^9/L in group III. In groups I and II increases in reticulocyte counts were significant compared with group III on the 1st and 7th days ($p < 0.01$). However, reticulocyte counts decreased thereafter in groups I and II resulting in significant decreases on day 21 compared with group III ($p < 0.01$).

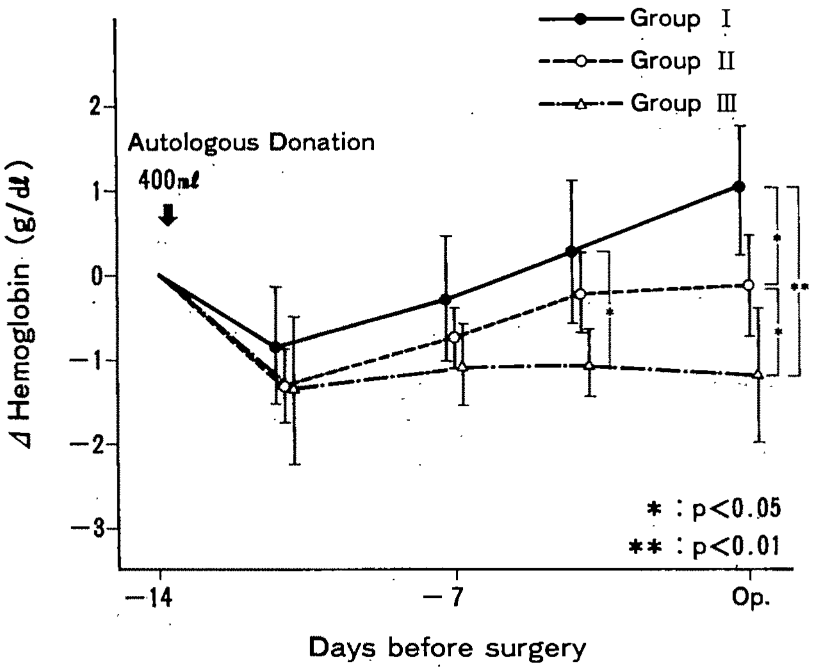

Fig 2. Changes in hemoglobin levels before operation. The hemoglobin levels in group I (administration of recombinant human erythropoietin [rHuEPO] and iron) and group II (administration of rHuEPO only) recover better than those in group III (control), and that in group I, significantly better than in group II. (ΔHemoglobin = the differences between hemoglobin levels before autologous blood collection and thereafter; Op. = the day of operation.)

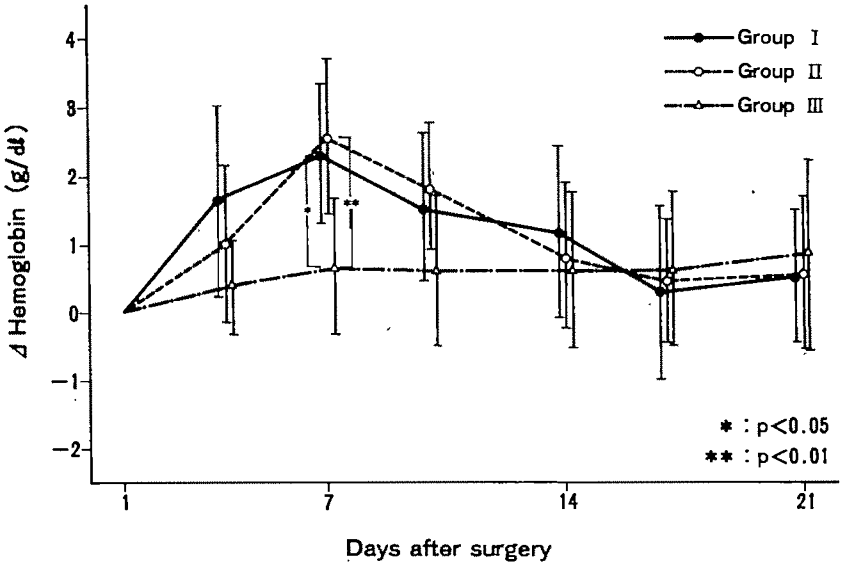

*Fig 3. Changes in hemoglobin levels after operation. In group I and group II the hemoglobin levels increase significantly during the administration of rHuEPO. Note the rapid decrease of the hemoglobin levels after discontinuing rHuEPO at the seventh postoperative day. (*ΔHemoglobin = *the differences between hemoglobin levels determined the first day after operation and thereafter.)*

In groups I and II serum iron levels decreased significantly compared with group III starting on the seventh day before operation, but there were no significant differences between groups I and II (Fig 5). Serum iron levels were comparable among the three groups after operation.

There were no significant differences among the three groups with respect to platelet and leukocyte levels.

Comment

Erythropoietin, a hematopoietic hormone, was first isolated and purified by Miyake and associates [3] in 1977. Since Jacobs and co-workers [4] and Lin and colleagues [5] succeeded in cloning the erythropoietin gene in 1985, large-scale production of rHuEPO has become possible using recombinant DNA technologies. Recombinant human erythropoietin was subsequently administered to patients with chronic renal anemia and was found to be effective in improving the anemia induced by renal failure [6–9]. At present, efforts are being made to use rHuEPO in conjunction with the collection of autologous blood before elective operations. Levine and associates [10] reported the efficacy of rHuEPO in a phlebotomy experiment in baboons conducted as a part of basic studies into this clinical application. In humans, rHuEPO has been used in this indication by some investigators in the field of orthopedic surgery [11, 12].

In this study we used rHuEPO before and after open

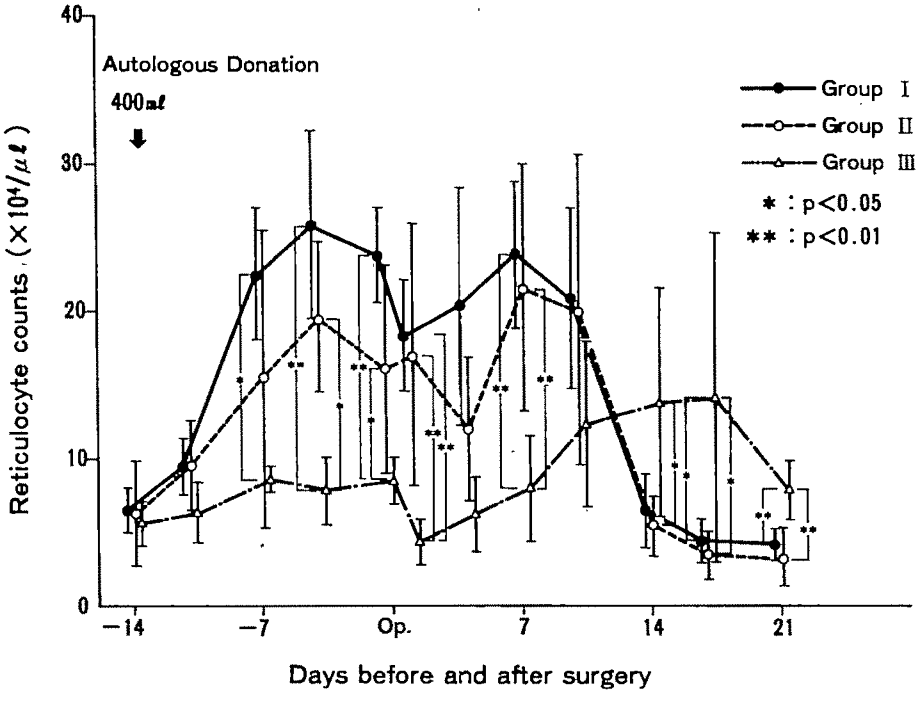

*Fig 4. Changes in reticulocyte counts. (*Op. = *the day of operation.)*

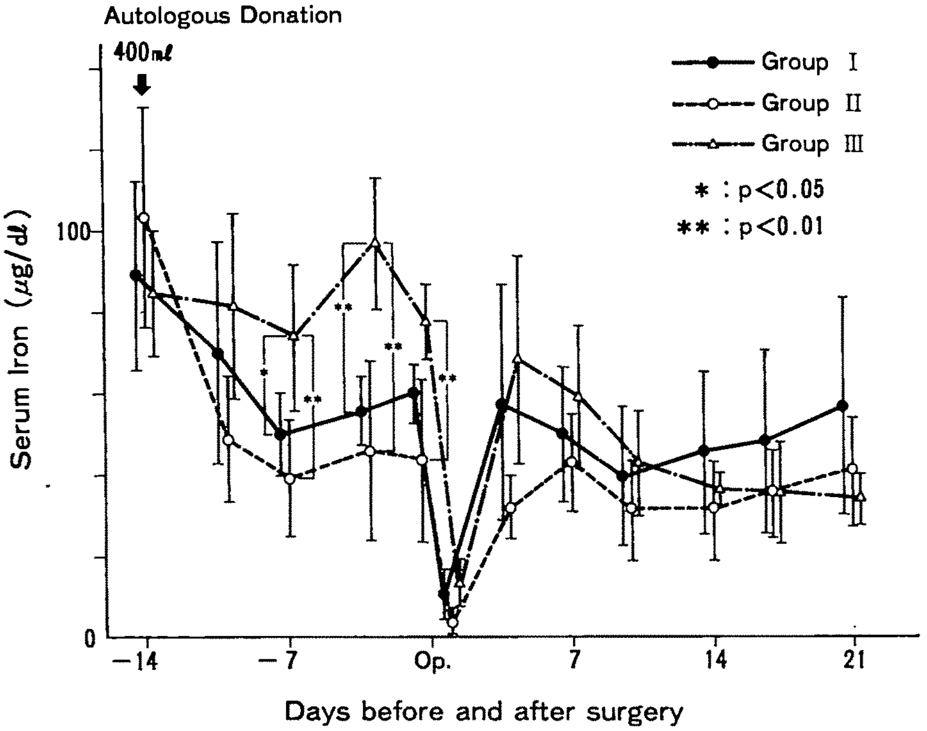

Fig 5. Changes in serum iron levels. (Op. = the day of operation.)

heart operations and studied its effect on improving the anemia associated with preoperative autologous blood collection and on improving postoperative anemia. As a control group, past patients in whom open heart operations were performed with autologous blood transfusion but without using rHuEPO were compared.

Increases in hemoglobin levels over the 2 weeks after collection of 400 mL of autologous blood were significantly greater in patients treated with rHuEPO compared with the control. Concomitant administration of iron preparations enhanced the effects of rHuEPO. Serum iron levels decreased significantly after administration of rHuEPO compared with the control, a finding that suggests increases in the utilization of iron by rHuEPO. Although there were no significant differences in the serum iron levels between the group given rHuEPO alone and that given rHuEPO and iron, concomitant administration of iron seems necessary regardless of serum iron levels. Further studies are needed to determine the dosage and method of administration of iron. In patients given rHuEPO along with iron, the hemoglobin levels returned to baseline within 10 days after collection of 400 mL of autologous blood. Hemoglobin levels further increased to about 10 g/L 14 days after collection, suggesting that it is possible to withdraw an additional 400 mL of blood before operation. Recombinant human erythropoietin offers great advantages if it makes it possible to obtain 800 mL of autologous blood within 2 weeks, which is the volume usually required to avoid any homologous blood transfusion.

After operation, improvement in anemia was obvious during the treatment with rHuEPO. Upon the termination of the treatment on the seventh day after operation, however, hemoglobin levels started to decrease, ranging from 11 to 18 g/L 1 week after the termination of the therapy and becoming comparable with the control on day 21 after operation. Few studies have been conducted on changes in erythrocytes after the termination of rHuEPO treatment. In chronic treatment in patients with renal failure, erythrocyte count was found to decrease gradually after the termination of the treatment [8]. In this study, there were rapid decreases in hemoglobin levels after the discontinuation of the acute treatment with rHuEPO. Reticulocyte levels started to increase about 7 days after treatment with rHuEPO, remained at high levels during the treatment period, and returned to baseline about 7 days after the termination of the treatment. This rapid decrease in reticulocyte levels upon the termination of the treatment may be attributable to the inhibition of endogenous erythropoietin production, but this does not sufficiently explain the rapid decrease in hemoglobin levels. Further studies are needed to confirm the effects of rHuEPO on postoperative anemia.

The following conclusions were obtained from the findings in the present study: (1) rHuEPO was effective in ameliorating the anemia associated with autologous blood collection before open heart operation. The effect was further enhanced by intravenous supplementing iron preparations. (2) Although rHuEPO was effective in improving anemia over a short period after open heart operation, hemoglobin levels decreased rapidly upon the termination of the treatment.

Recombinant human erythropoietin was produced and provided by the Kirin Brewery Co, Ltd, Tokyo, Japan.

References

1. Shibata Y, Kawabata M, Fuse K. Experience with the use of autologous frozen blood in 100 patients. Low Temp Med 1988;14:53–5.
2. Chinchlli VM. Clinical efficacy trials with quantitative data. In: Peace KE. Biopharmaceutical statistics for drug development. New York, Basel: Marcel Dekker, 1988:353.
3. Miyake T, Kung CKH, Goldwasser E. Purification of human erythropoietin. J Biol Chem 1977;252:5558–64.
4. Jacobs K, Shoemaker C, Rudersdorf R, et al. Isolation and characterization of genomic and cDNA clones of human erythropoietin. Nature 1985;313:806–10.
5. Lin FK, Suggs S, Lin CH, et al. Cloning and expression of the human erythropoietin gene. Proc Natl Acad Sci USA 1985; 82:7580–4.
6. Winearls CG, Oliver DO, Pippard MJ, Reid C, Downing MR, Cotes PM. Effect of human erythropoietin derived from recombinant DNA on the anaemia of patients maintained by chronic haemodialysis. Lancet 1986;2:1175–8.
7. Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. N Engl J Med 1987;316: 73–8.
8. Akizawa T, Koshikawa S, Takaku F, et al. Clinical effect of recombinant human erythropoietin on anemia associated with chronic renal failure. A multi-institutional study in Japan. Int J Artif Organs 1988;11:343–50.
9. Eschbach JW, Kelly MR, Haley NR, Abels RI, Adamson JW. Treatment of the anemia of progressive renal failure with recombinant human erythropoietin. N Engl J Med 1989;321: 158–63.
10. Levine EA, Rosen AL, Gould SA, et al. Recombinant human erythropoietin and autologous blood donation. Surgery 1988; 104:365–9.
11. Goodnough LT, Rudnick S, Price TH, et al. Increased preoperative collection of autologous blood with recombinant human erythropoietin therapy. N Engl J Med 1989;321: 1163–8.
12. Maeda H, Hitomi Y, Hirata R, et al. Erythropoietin and autologous blood donation. Lancet 1989;2:284.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1993 may begin the recertification process in 1991. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is July 1, 1991. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Delayed Sternal Closure for Life-Threatening Complications in Cardiac Operations: An Update

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Over a 7-year-period, 25 patients had delayed sternal closure after open heart operations out of 34 patients whose sternum was not closed. The indications were extreme cardiac dilatation and uncontrollable mediastinal hemorrhage. This represented a 1.79% incidence in the overall open heart surgical experience at our unit. Sternal closure was performed at a mean of 2.64 days after the initial operation. Eighteen patients (52.9%) left the hospital alive and well, representing a 72% survival rate among patients undergoing delayed sternal closure. No mediastinal or fatal infection developed and only 1 patient had late superficial wound infection after delayed sternal closure. We conclude that delayed sternal closure is an effective method to treat severe complications after cardiac operations.

(Ann Thorac Surg 1991;51:773–6)

Myocardial edema and intraoperative bleeding are two severe complications secondary to prolonged cardiopulmonary bypass and aortic cross-clamping time. Although cardiomegaly and bleeding seldom prevent primary approximation of both sternal halves, continued mediastinal bleeding and compression of the heart resembling cardiac tamponade can pose problems: when and how to close the sternum and how to isolate the mediastinum from the environment if primary sternal closure has to be delayed [1–7].

These situations are, fortunately, rare. The need to delay the closure of the sternum is difficult to estimate; however, data from Gielchinsky [3], Fanning [6], Josa [8], and their associates, taken from retrospective studies, give an overall incidence of 1.5%, 1.7%, and 2.8%, respectively. Conventional primary sternal wiring should be attempted at the end of a cardiac operation. However, hemodynamic impairment and uncontrollable bleeding in critically ill patients or the need for additional cannulations because of mechanical cardiac support may mandate leaving the sternum open. The incidence is low and the overall reported experience is still scanty, especially when compared with the enormous amount of open heart operations performed worldwide [3, 6, 8].

We would like to comment on our current experience in this field by reporting on 34 patients in whom the sternum was initially left open, after all efforts to improve patient status including maximal inotropic and mechanical support or all hemostatic agents were used. Twenty-five patients subsequently underwent delayed sternal closure (DSC) as a method to treat intraoperative life-threatening complications after cardiac operations.

Material and Methods

From January 1983 until March 1990, 1,900 open heart operations were performed at our unit. In 34 cases (1.79%) different severe intraoperative conditions precluded primary wiring of the sternum. Nine patients were extremely ill at the time of leaving the operating room and died in the intensive care unit between 3 hours and 4 days after the operation with the chest still open. The cause of death in these nonsurvivors was low cardiac output in 6, intractable arrhythmia in 2, and bowel infarction in 1. The remaining 25 patients were managed by DSC.

There were 20 male and 14 female patients, ages ranging from 7 to 81 years (mean age, 53.29 ± 17.68 years). Operations performed included valve replacement in 16 patients, coronary bypass grafting in 10, operation for the complications of acute myocardial infarction in 3 (including repair of cardiac rupture, closure of a ventricular septal defect, and repair of a left ventricular aneurysm), repair of type A aortic dissection in 2, and mitral commissurotomy, right ventricular outflow tract patching, and resection of subaortic stenosis in 1 each. Nine patients (26.5%) were undergoing redo cardiac operations. The procedures were performed employing standard techniques of cardiopulmonary bypass. Cold hyperkalemic crystalloid cardioplegia and pericardial lavage with cold saline solution was the method of myocardial preservation. In this group of patients, bypass time ranged from 87 to 340 minutes (mean, 158.20 ± 53.78 minutes) and aortic cross-clamping time ranged from 20 to 170 minutes (mean, 79.96 ± 36.5 minutes). Intraaortic balloon counterpulsation was required in 6 patients and 3 patients required right (2) and left (1) ventricular assistance with paracorporeal devices (1 roller pump, 1 centrifugal pump, and 1 pneumatically driven assist pump).

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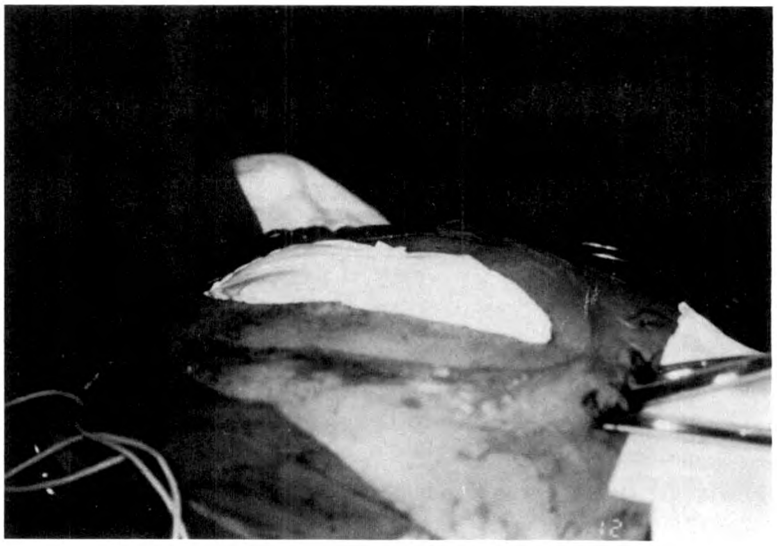


Fig 1. Postoperative view of a patient (who later underwent delayed sternal closure) at the time of initially leaving the operating room after a complicated procedure. The Gore-Tex Surgical Membrane was used to cover the skin defect.

Indications for Delayed Sternal Closure

UNCONTROLLABLE HEMORRHAGE. Coagulopathy leading to uncontrollable bleeding was the indication for DSC in 16 patients in the group, including 1 patient in whom an allergic reaction to protamine developed. In these patients, standard methods of hemostasis were attempted including topical hemostatic agents and massive transfusion of bank blood, fresh frozen plasma, platelets, and cryoprecipitate. Finally, together with the connection of large-bore mediastinal tubes to a Cell Saver unit, mediastinal packing with dry gauze soaked in iodine-povidone was performed.

CARDIAC COMPRESSION. Delayed sternal closure was indicated because of cardiac compression in 14 patients. Hemodynamic deterioration was seen at the time of sternal approximation because of severe myocardial edema and subsequent increase in cardiac size. The inability to maintain good hemodynamic status, with systemic hypotension and low cardiac output, led us to leave the sternum open. Low cardiac output was managed with vasodilators and inotropic agents, intraaortic balloon pumping, and different types of ventricular assist devices. An additional indication was the extra space required for nonstandard cannulations.

Mediastinal Isolation

The problem of what to do to isolate the mediastinum from the environment is as important as the decision to leave the sternum open. The risk of a mediastinal infection is very high under these conditions. In this series we were able to approximate the skin in 8 patients; in 24 patients synthetic membranes (21 patients, Gore-Tex Surgical Membrane [W. L. Gore & Assoc, Flagstaff, AZ]; 3 patients, Mitrathane Cardiac Patch [Mitral Medical of Canada, Wheat Ridge, CO]) were used to cover the mediastinal gap and were sutured to the skin edges; in 2 patients the surgical wound was left open and the defect simply covered by a plastic drape (Steri-Drape; 3M, Medical Surgical Division, St. Paul, MN). Perioperative antibiotic coverage consisted of cephalosporine dosage before induction and every 6 to 8 hours according to the antibiotic used (cefamandole or cefuroxime sodium) (Fig 1). All patients were kept paralyzed and sedated in an attempt to optimize hemodynamics and prevent cannular dislodgement when assist devices were used. No stents were used to hold the sternum apart. We found no need to use stents among our adult population. This practice seems to be more common in pediatric cardiac operations when dealing with DSC. No mediastinal irrigation was used.

Results

As mentioned, 9 patients (26.4%) were extremely ill at the time of leaving the operating room and died in the intensive care unit between 3 hours and 4 days after the operation with the chest still open. In this group are included the 3 patients on mechanical ventricular assistance.

Sternal Closure

When the hemodynamic condition was stable or when mediastinal bleeding stopped, the remaining 25 patients were returned to the operating room for sternal wiring. The improvement in hemodynamics included stable blood arterial pressure and pulmonary artery pressure, improved urine output, and substantial weaning from inotropes. At that time, the patients were considered able to tolerate sternal closure. Delayed sternal closure was performed between 1 and 4 days (mean, 2.64 ± 1.07 days) after the operation. Findings at the time of DSC were the reduction of cardiac size in the patients left open because of myocardial edema and the absence of mediastinal bleeding with the pads being adherent in the mediastinum in those patients who bled. No problems were noted at the time of removal of the mediastinal pack in any patient. No serious air leaks were noted through the suture line of the synthetic membranes used to cover the skin gap during the period before DSC.

Complications

In no patient did mediastinitis or fatal infection related to DSC develop. One patient (4%) undergoing successful DSC for cardiac compression later had a superficial wound infection (*Pseudomonas aeruginosa*) that required readmission 3 months after admission. He was managed by systemic antibiotics, wound debridement, and removal of sternal wires with excellent results. That late complication perhaps could be properly attributed to the technqiue itself. In another patient, catheter-related sepsis (enterococcus) and urine infection (*Escherichia coli*) developed, which were controlled by antibiotics. These two additional infectious complications are obviously not related to the DSC procedure.

Mortality

Eighteen patients left the hospital alive and in good condition, representing 52.9% of the overall group and 72% of the patients finally undergoing DSC. Among the survivors, in 12 we used patches to cover the skin and in 6 we directly closed the skin or we left it open. Mortality figures for the two types of closure were thus 47.1% and 28%, respectively. The cause of death after DSC was multiorgan failure in 4 patients and reinfarction, pulmonary embolus, and catheter-induced sepsis in 1 each.

Comment

Both uncontrollable bleeding secondary to postbypass coagulopathy and increased cardiac size due to generalized myocardial edema can preclude primary sternal closure at the end of cardiac operations. Intraoperative noncardiogenic pulmonary edema and intractable arrhythmia developing in complicated cases can also be a cause to delay closure of the sternum. Although primary closure of the chest wall should be attempted, this is sometimes not possible. Riahi and associates [9] are credited as the first to recognize and treat the phenomenon of cardiac compression due to a disproportion between cardiac size and mediastinal space. This problem was solved in their report by external orthopedic sternal traction. Some other authors used different techniques trying to increase mediastinal size and to isolate the mediastinum from the environment, techniques that included skin approximation [3] or the use of rubber or Dacron sheets [2, 10, 11].

Restriction of diastolic filling is the main event when there is a disproportion in the cardiomediastinal relationship leading to compression and tamponade [3, 5]. Excessive myocardial edema can lead to this complication. Severe pulmonary emphysema can act in a similar way by compressing the heart.

On the other hand, bleeding unresponsive to conventional replacement therapy including massive transfusion of bank blood, fresh frozen plasma, platelets, and coagulation factors and administration of topical hemostatic agents can be sometimes managed only by mediastinal drainage and packing with dry gauze. In both situations, disproportion between the cardiac size and the mediastinal space is the rule and the sternum cannot be closed because of the deleterious hemodynamic consequences. Delayed sternal closure would help to avoid this discrepancy in size and allow the recovery of cardiac function and stop bleeding.

Today, an additional situation that can be an indication for DSC is the space needed for nonconventional cannulations. An intraaortic balloon placed through the ascending aorta in the presence of peripheral arterial occlusive disease can also create size discrepancies within the mediastinum according to the technique of insertion. The same can occur when ventricular assist devices (right or left) must be implanted because of univentricular or biventricular heart failure. Large cannulas needed to connect the patient to a paracorporeal assist device can fill the retrosternal space. Delayed sternal closure could be the solution to the space required for additional cannulations, as pointed out by Gielchinsky and associates [3] and O'Neill and co-workers [12]. That was our experience with 4 patients, 3 with paracorporeal devices and 1 with an intraaortic balloon pump inserted through the ascending aorta.

Mediastinal infection is a life-threatening complication after open heart operations [13]. The risk of deep infection when DSC is indicated is very high because the natural barrier between the mediastinum and the environment is altered. This is one of the determinants of the reluctance of surgeons to leave the chest open. Several solutions to close the defect have been tested. Approximation of the skin as described by Gielchinsky and associates [3] is the most logical approach, but is not always possible. Other approaches to cover the skin defect have been advocated. Standard adhesive surgical drapes seem not to be the ideal method because they do not completely seal the wound. Continuous oozing and also the need to change the dressing several times a day may compromise the expected sterile conditions required to manage an open postsurgical mediastinum. Rubber sheets are advocated by Josa and colleagues [8]. We used synthetic membranes; in 24 patients we placed 34 Gore-Tex Surgical Membranes and 3 Mitrathane Cardiac Patches to cover the wounds because most patients required more than one membrane to cover the defect. These membranes were sutured to the skin edges and effectively acted as a barrier to protect the mediastinum. In fact, no evidence of mediastinal infection was noted in these patients.

The analysis of the Gore-Tex Surgical Membrane showed no bacterial growth after an average of 3 ± 1 days of implantation in the 5 patients from whom they were retrieved at the time of DSC. In spite of the fact that the Mitrathane Cardiac Patch and the Gore-Tex Surgical Membrane were initially designed for other specific applications such as pericardial closure [14, 15], we believe that temporary skin closure at the time of DSC could be a secondary indication for the use of such membranes, especially the Gore-Tex Surgical Membrane because the Mitrathane patch is no longer available.

Infectious local complications have been seldom seen in our series of 25 patients finally treated by DSC. Only 1 patient had a superficial wound infection; 3 months after operation he required readmission to start antibiotic therapy and surgical removal of sternal wires, and no mediastinal infection developed. Local infectious complications have also been very infrequent or absent in the small number of patients recorded in the published series.

The decision of when to close the sternum must be individualized in each patient. Cessation of active bleeding or a substantial improvement in hemodynamics with the use of conventional mechanical or pharmacological methods (vasodilators, inotropics, diuretics) and negative water balance will indicate the timing of sternal closure. Obviously, no strict rules can be applied.

Delayed sternal closure has not received much attention in the literature, as only a few reports, including 160 cases, have been published since 1975 [1–6, 8, 10–12, 16–18]. It has proved to be an effective method of treatment of severe intraoperative life-threatening complications in open heart operation in our hands, with a 72% survival rate in critically ill patients in whom it is accomplished. We advise for its reasoned and judicious application. The use of synthetic membranes to temporarily cover the skin defect is also recommended both for patients with coagulation defects and for patients with cardiac dysfunction, because of the excellent results obtained with regard to the isolation of the mediastinum and the absence of severe infectious complications. In spite of our present experience, we believe that the use of synthetic membranes should not be a routine, and that it has to be individually considered in each particular case. Our present policy is to approximate the skin but, if cardiac compression develops, we leave the skin open and implant a synthetic membrane.

We sincerely appreciate the cooperation given by C. N. Lee, MBBS, FRACS, in his kind manuscript review.

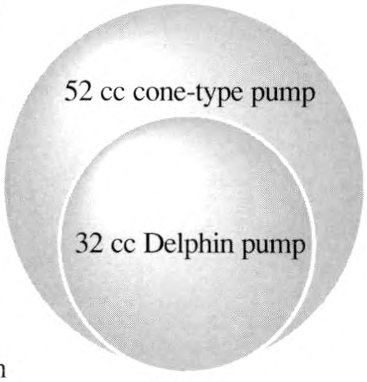
References

1. Culliford AT, Thomas S, Spencer FC. Fulminating noncardiogenic pulmonary edema: a newly recognized hazard during cardiac operations. J Thorac Cardiovasc Surg 1980;80:868–75.
2. Gangahar DM, McGough EC, Synhorst D. Secondary sternal closure: a method of preventing cardiac compression. Ann Thorac Surg 1981;31:281–2.
3. Gielchinsky I, Parsonnet V, Krishnan B, Silidker M, Abel RM. Delayed sternal closure following open-heart operation. Ann Thorac Surg 1981;32:273–7.
4. Björk VO, Papaconstantinou C. Delayed sternal closure following cardiac operation. Scand J Thorac Cardiovasc Surg 1982;16:275–7.
5. Jogi P, Werner O. Hemodynamic effects of sternum closure after open-heart surgery in infant and children. Scand J Thorac Cardiovasc Surg 1985;19:217–20.
6. Fanning WJ, Vasko JS, Kilman JW. Delayed sternal closure after cardiac surgery. Ann Thorac Surg 1987;44:169–72.
7. Igual A, Murtra M, Salas A, Figueras J. Reapertura esternal y cierre diferido como tratamiento del sindrome de compresion cardiac postquirurgico. Rev Esp Cardiol 1988;41:192–3.
8. Josa M, Khuri S, Braunwald NS, et al. Delayed sternal closure—an improved method of dealing with complications after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1986;91:589–603.
9. Riahi M, Tomatis LA, Schlosser RJ, Bertolozzi E, Johnston DW. Cardiac compression due to closure of median sternotomy in open-heart surgery. Chest 1975;67:113–4.
10. Martinez MJ, Albus RA, Barry MJ, Bowen TE. Treatment of cardiac compression after cardiopulmonary bypass. Am J Surg 1984;147:400–1.
11. Murphy DA. Delayed closure of the median sternotomy incision. Ann Thorac Surg 1985;40:76–7.
12. O'Neill MJ, Pierce WS, Wisman CB. Successful management of right ventricular failure with ventricular assist pump following aortic valve replacement and coronary bypass grafting. J Thorac Cardiovasc Surg 1984;87:106–11.
13. Serry C, Bleck PC, Javid H, et al. Sternal wound complications. Management and results. J Thorac Cardiovasc Surg 1980;80:861–7.
14. Mestres CA, Comas JV, Ninot S, et al. The use of polyetherurethane urea (Mitrathane) and polytetrafluoroethylene (Gore-Tex) membranes for pericardial closure: initial clinical results. Thai J Surg 1985;7:125–8.
15. Revuelta JM, Garcia-Rinaldi R, Val F, et al. Expanded polytetrafluoroethylene surgical membrane for pericardial closure. J Thorac Cardiovasc Surg 1985;89:541–5.
16. Milgalter E, Uretzky G, Shimon D, Silberman S, Appelbaum A, Borman JB. Delayed sternal closure following cardiac operations. J Cardiovasc Surg 1986;27:328–31.
17. Ott DA, Cooley DA, Norman JC, Sandiford FM. Delayed sternal closure: a useful technique to prevent tamponade or compression of the heart. Cardiovasc Dis (Bull Tex Heart Inst) 1978;5:15–8.
18. Ugorji CC, Turner SA, McGee MG. Transascending aortic intraaortic balloon insertion with delayed sternal closure: a retrospective analysis. Cardiovasc Dis (Bull Tex Heart Inst) 1980;7:307–15.

Air handling and centrifugal blood pumps

By far the most popular reason given for using centrifugal pumps is safety.[1] Certainly, the inability to pump gross air (a large bolus of air) is a significant safety advantage of centrifugal pumps. Yet not all centrifugal pumps perform equally well when it comes to air handling.

Protection against gross air



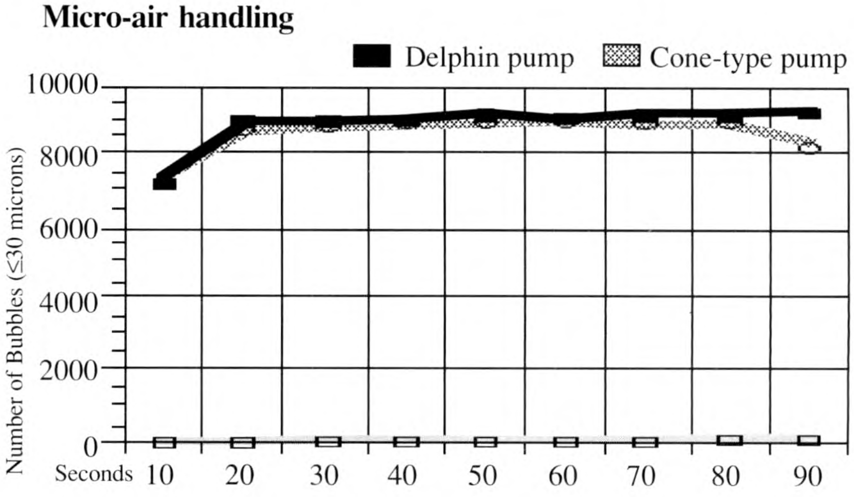
Air to deprime

A large bolus of air will deprime a centrifugal pumphead. Once the pump is deprimed, the flow rate drops to 0 and the air is held up in the pumphead, though the pump continues to spin. Roller pumps, on the other hand, will continue to force air on towards the patient.

Just 32 cc of air will deprime a Delphin pumphead. Approximately 52 cc are required to deprime a cone-type centrifugal pump.[2] The Delphin pumphead protects patients by depriming with a relatively small amount of air.

Micro-air handling

All arterial pumps, including centrifugal pumps, will pump micro-air to some extent.[3] Under similar operating conditions, centrifugal pumps are essentially equivalent in their micro-air handling abilities.[4]

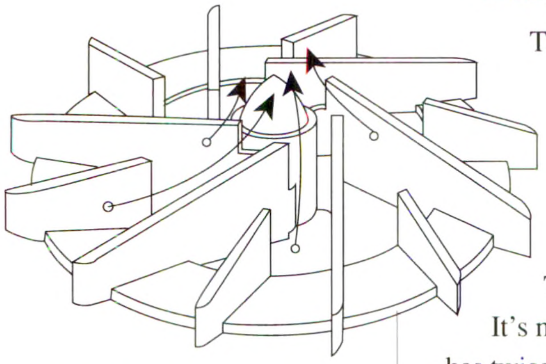


Although micro-air handling is essentially equivalent for all centrifugal pumps (as shown on this graph), the Delphin system deprimes with only 32 cc of air.

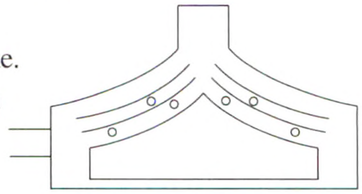
Easy debubbling

The open impeller design of the Delphin pumphead lends itself to convenient debubbling. Bubbles trapped beneath the cones are difficult to remove during priming. In an effort to debubble, many perfusionists resort to vigorously tapping the cone-type pumphead, a practice one manufacturer warns "may cause device malfunction."

Tap the Delphin pumphead if you like. It's made of durable polycarbonate which has twice the impact strength of the acrylic used in some pumpheads[5].



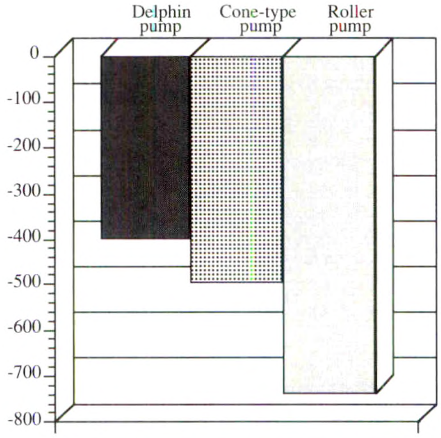
The open impeller design of the Delphin pumphead facilitates debubbling.



The constrained design of cone-type pumpheads tends to trap bubbles during priming.

What about cavitation?

Cavitation, the sudden formation of micro-bubbles in solution, is caused by negative pressure. The greater the negative pressure potential at the pump inlet, the greater the risk of cavitation. Conversely, the lower the negative pressure, the greater the protection against cavitation. The Delphin system provides protection against cavitation by generating low levels of negative pressure. Should the inlet be occluded, the Delphin system produces less negative pressure than other pumping systems (for equivalent flow rates and pressure readings).



Negative pressure generated
(inlet occluded at 4L/min and 400 mm Hg)

The Delphin pump protects against cavitation by generating low levels of negative pressure.

For more information about centrifugal pumps, or a free, no-obligation clinical evaluation of the Delphin centrifugal system, call **800/521-2818**. Or write Sarns, 3M Health Care, 6200 Jackson Road, Ann Arbor, MI 48103.

Footnotes

[1] Based on a poll of *Heart-To-Heart* readers conducted in June, 1990. Almost three out of four respondents were already using a centrifugal pump for arterial perfusion (67%) or planned to (7%). A solid 26% did not use centrifugal pumps at all, and 15% were infrequent users.

[2] Pumps were flowing at 3.5 L/min with a pump outlet pressure of 300 mm Hg, a static pressure head of 30 mm Hg, and a mean arterial pressure of 60 mm Hg. To obtain these flow rates and pressures, the Delphin pump was operating at 2,350 RPMs, and the cone-type pump at 2,800 RPMs.

[3] Reed, Charles C. and Stafford, Trudi B. *Cardiopulmonary Bypass*. Houston: Texas Medical Press, Inc., 1985, p. 377.

[4] Numbers of 30 micron micro-bubbles were counted using a TLL Micro-bubble Activity Monitor attached near the centrifugal pump outlets following the introduction of 10 cc of air into each pumphead.

[5] Based on Izod impact of plastics testing for polycarbonate and acrylic using ASTM test method D256.

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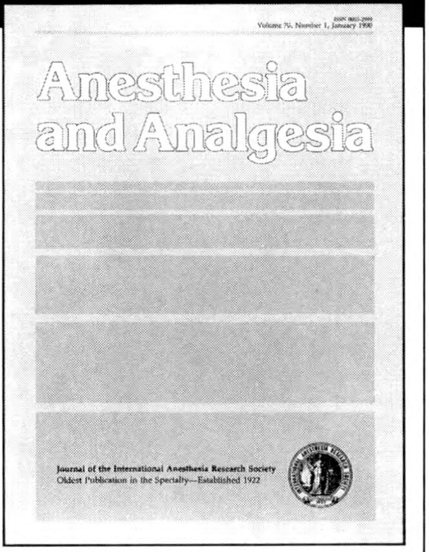

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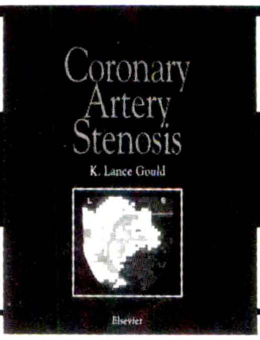

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Oxygenation of Cardioplegic Solutions: A Note of Caution

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The merits of oxygenated crystalloid cardioplegic solutions have been well established in experimental animals. The positive effects of oxygenation of Plasmalyte B (Sabax Ltd) and St. Thomas Hospital solution (Plegisol) were achieved by gassing with 95% O_2/5% CO_2 and 100% O_2, respectively. In view of the marked pH differences induced by these gas mixtures, we evaluated the effect of mode of oxygenation on myocardial recovery during reperfusion after hypothermic cardioplegic arrest. Oxygenation with 100% O_2 of Plasmalyte B containing high K^+ levels caused marked deterioration in myocardial recovery, whereas the mode of oxygenation did not affect recovery after arrest with St. Thomas Hospital solution. Because the major differences between these solutions reside in their respective K^+, Mg^{2+}, and HCO_3^- contents, the effects of variations in the levels of these ions were investigated. The results showed that oxygenation with 100% O_2 was deleterious only in the presence of high K^+ (29 mmol/L), low Mg^{2+} (3 mmol/L), and high $NaHCO_3$ (28 mmol/L) levels. The marked decline in mechanical recovery during reperfusion was associated with significant changes in myocardial adenosine triphosphate and intracellular Ca^{2+} levels. Although an explanation for these findings is not readily available, it is suggested that complex ionic interactions and possibly oxygen free radical generation may lead to intracellular Ca^{2+} overload, depression in mitochondrial adenosine triphosphate generation, and, hence, deterioration in mechanical recovery.

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The merits of an oxygenated crystalloid cardioplegic solution have been well established from experimental work in dogs [1] as well as in the isolated rat heart [2–4]. It was also demonstrated that the percentage recovery during reperfusion was dependent on the oxygen tension of the cardioplegic fluid [3]. The positive effects of oxygenation of Plasmalyte B (Sabax Ltd; Johannesburg, Republic of South Africa) and St. Thomas Hospital solution (Plegisol; Abbott Laboratories, North Chicago, IL) were achieved by gassing with 95% O_2/5% CO_2 [2, 3] and 100% O_2 [4], respectively. In view of the marked differences in pH induced by these two gas mixtures, it was decided to evaluate the effect of mode of oxygenation on myocardial recovery during reperfusion after hypothermic cardioplegic arrest. Preliminary experiments showed that oxygenation with 100% O_2 of Plasmalyte B containing high K^+ levels caused marked deterioration in myocardial recovery, whereas the mode of oxygenation did not affect mechanical recovery during reperfusion after cardioplegic arrest with St. Thomas Hospital solution. To find an explanation for these perplexing findings, the effects of oxygenation with 95% O_2/5% CO_2 and 100% O_2 were evaluated in different formulations of Plasmalyte B and St. Thomas Hospital solution. Because the major differences between these two cardioplegic solutions reside in their respective K^+, Mg^{2+}, and HCO_3^- contents [2, 3, 5], the effect of variations in the levels of these ions was investigated.

Material and Methods

Animals

Male Wistar rats (225 to 250 g), fed *ad libitum,* were used in all experiments. Animals were cared for according to national and institutional guidelines for humane animal care. Animals were anesthetized with pentobarbital (30 mg/kg) given intraperitoneally.

Perfusion Technique

After the heart was removed, it was mounted onto the aortic cannula and perfused retrogradely for 10 minutes with Krebs-Henseleit buffer (pressure, 80 mm Hg; 37°C) during which time the left atrium was cannulated. The heart was then converted into a working heart model for 20 minutes according to the method of Neely and associates [6] as modified by Opie and co-workers [7]. The left atrial filling pressure was maintained at 15 cm H_2O and afterload at 100 cm H_2O. During this period at least two measurements of the aorta and coronary flow rates were made, and aortic pressure was recorded with a Statham P23 D6 pressure transducer.

After the 20-minute control perfusion period, hearts were switched to a system that allowed for administration of the cold cardioplegic solution. Hearts were arrested with cardioplegic solution administered at 20°C for a

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Table 1. Composition of Cardioplegic Solutions

Component[a]	Plasmalyte BI (high K^+)	Plasmalyte BII (high K^+, high Mg^{2+})	Plasmalyte BIII (low K^+)	Plasmalyte BIV (low K^+, high Mg^{2+})	St. Thomas Hospital solution I	St. Thomas Hospital solution II (high K^+)	St. Thomas Hospital solution III (high K^+, low Mg^{2+})	St. Thomas Hospital solution IV (high K^+, low Mg^{2+}, high HCO_3^-)
NaCl	102	102	102	102	110	110	110	110
KCl	29	29	16	16	16	29	29	29
$MgCl_2$	3	16	3	16	16	16	3	3
$CaCl_2$	1.25	1.25	1.25	1.25	1.20	1.20	1.20	1.20
$NaHCO_3$	28	28	28	28	10	10	10	28
pH	7.4	7.4	7.4	7.4	7.8	7.8	7.8	7.8
Osmolality (mOsm/kg H_2O)	287	320	273	280	297	320	286	321

[a] Values are given in millimoles per liter. [b] KCl, $MgCl_2$, and $CaCl_2$ were added to Plasmalyte B.

period of 2 minutes (pressure, 40 mm Hg). The cardioplegic solutions were continuously gassed with either 95% O_2/5% CO_2 or 100% O_2 for the duration of the cardioplegic period. The hearts were intermittently perfused for 3 minutes at 30-minute intervals over a 2-hour period. Measurements of pH, oxygen tension, and carbon dioxide tension (at 37°C) were made simultaneously at each 30-minute interval using a Corning 168 pH/blood gas analyzer (Medfield, MA). Accurate temperature control was achieved by surrounding the heart with a double-walled glass chamber kept at 20°C by a Lauda K4R Electronic circulating water bath. At the end of the hypothermic cardioplegia, the hearts were reperfused retrogradely for 10 minutes with Krebs-Henseleit buffer at 37°C before being switched to the working heart model for another 20 minutes. At least two measurements each of coronary and aortic flow rates as well as recordings of aortic pressure were made during this period. Work performance was calculated according to the technique described by Kannengieser and associates [8]:

$$\text{Pressure power} = 0.002222 \times \text{PSP} \times \text{CO}$$

$$\text{Kinetic power} = \frac{P}{432 \times 10^7} \times \frac{\text{CO}^3}{A^2} \times \frac{T^2}{\text{Te}}$$

where CO = cardiac output (mL/min); PSP = peak systolic pressure (mm Hg); A = cannula internal cross-sectional area (mm^2); P = density of perfusate (mL/g); T = cycle time (s); and Te = ejection time (s).

Both the Krebs-Henseleit buffer and the cardioplegic solutions were filtered before use through a 0.45-μm Millipore filter. No precipitate was formed during oxygenation of the cardioplegic fluid. The composition of the Krebs-Henseleit buffer was as follows (in mmol/L): NaCl, 119; $NaHCO_3$, 24.9; KCl, 4.74; KH_2PO_4, 1.19; $MgSO_4$, 0.6; Na_2SO_4, 0.59; $CaCl_2$, 1.25; glucose, 10. The composition of the eight different cardioplegic solutions is summarized in Table 1. $CaCl_2$, KCl, and $MgCl_2$ were added to commercially available Plasmalyte B (Sabax Ltd). The composition of unmodified Plasmalyte B is as follows (in mmol/L): NaCl, 102; KCl, 4; $MgCl_2$, 3; $NaHCO_3$, 28; pH, 7.4.

Tissue Analysis

For measurement of tissue high-energy phosphate contents, hearts were freeze-clamped with Wollenberger tongs at the end of the experimental period and stored in liquid nitrogen until extraction. A protein-free acid extract was prepared from 200 mg of pulverized frozen tissue according to the method of Gutman and Wahlefeld [9] and neutralized with KOH-Tris (40% KOH in saturated KCl [4 parts]; 0.2 M Tris-HCl, pH 7.5 [6 parts]). High-energy phosphates were analyzed by ion-pair reversed-phase high-performance liquid chromatography as described by Victor and colleagues [10].

Intracellular total calcium content of the ventricular myocardium was determined according to the technique described by Nayler and associates [11]. For removal of extracellular calcium the coronary vasculature was flushed through with 20 mL of a 0.35 mol/L sucrose–5 mmol/L histidine buffer (pH 7.4). This solution was initially passed through a Dowex cation exchange column (50 W). The hearts were dried for 48 hours at 100°C, weighed, and digested in 3 mL of concentrated HNO_3 for 48 hours. To assay for calcium, 0.5 mL of the extract was added to a calcium blank solution (27 mmol/L KCl; 27 μmol/L $LaCl_3$). The calcium content was determined by atomic absorption spectrophotometry (422.7 nm). A series of standard solutions was assayed simultaneously in the same manner.

Statistical Analysis

All results were expressed as mean ± standard error of the mean. Student's t test for unpaired data was used for data analysis, and p values less than 0.05 were considered significant.

Results

Effect of Oxygenation of Cardioplegic Fluid on Myocardial Recovery During Reperfusion

In these experiments each heart served as its own control. As expected, the control values obtained (ie, values obtained before induction of hypothermic arrest) in each

Table 2. Effect of Oxygenation of Plasmalyte BI (high K^+) on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	25	15.60 ± 0.70	48.80 ± 1.30	64.40 ± 1.70	94 ± 2	282 ± 4	0.23 ± 0.01	13.19 ± 0.39	0.32 ± 0.02	13.50 ± 0.41
Cardioplegia										
Nonoxygenated	6	11.10 ± 0.60^d	0^d	11.10 ± 0.60^d	76 ± 3^d	202 ± 18^d	0.056 ± 0.005^d	1.86 ± 0.10^d	0.01 ± 0.003^d	1.88 ± 0.10^d
95% O_2/5% CO_2	6	15.30 ± 2.10	30.40 ± 1.30^d	45.70 ± 1.90^d	83 ± 2^c	254 ± 9^b	0.18 ± 0.01^c	8.38 ± 0.33^d	0.15 ± 0.02^d	8.52 ± 0.35^d
100% O_2	13	11.00 ± 0.90^d	7.00 ± $3.00^{d,f}$	18.00 ± $4.00^{d,f}$	50 ± $11^{c,e}$	154 ± $36^{c,e}$	0.06 ± $0.02^{d,f}$	2.89 ± $1.00^{d,f}$	0.02 ± $0.01^{d,f}$	2.86 ± $0.99^{d,f}$

[a] Plasmalyte BI contains 29 mmol/L KCl (see Table 1). Values expressed as mean ± standard error of the mean. Significant difference between control and after-arrest values: [b] $p < 0.02$; [c] $p < 0.005$; [d] $p < 0.001$. Significant difference between after-arrest values for 95% O_2/5% CO_2 and 100% O_2: [e] $p < 0.005$; [f] $p < 0.001$.

HR = heart rate; PSP = peak systolic pressure; SV = stroke volume; W_k = kinetic work; W_p = pressure work; W_{Total} = total work.

Table 3. Myocardial Adenosine Triphosphate Content After Reperfusion of Hearts Arrested for 2 Hours at 20°C

Group	n	ATP Content (μmol/g dry weight)
Control[a]	5	20.35 ± 1.66
Cardioplegia		
Plasmalyte BI (high K^+)		
Nonoxygenated	5	15.03 ± 0.81^b
95% O_2/5% CO_2	6	20.62 ± 1.60
100% O_2	13	16.03 ± 1.90^c
Plasmalyte BII (high K^+, high Mg^{2+})		
95% O_2/5% CO_2	6	19.11 ± 2.67
100% O_2	8	17.88 ± 1.53
Plasmalyte BIII (low K^+)		
95% O_2/5% CO_2	7	20.33 ± 1.61
100% O_2	6	19.46 ± 2.59
St. Thomas Hospital Solution I		
Nonoxygenated	6	20.52 ± 1.68
95% O_2/5% CO_2	7	22.98 ± 2.18
100% O_2	6	20.26 ± 1.93
St. Thomas Hospital Solution II		
95% O_2/5% CO_2	6	16.74 ± 2.50
100% O_2	6	18.74 ± 0.86
St. Thomas Hospital Solution IV		
Nonoxygenated	6	9.21 ± 0.94^d
100% O_2	7	10.12 ± 1.40^d

[a] Control values were obtained from hearts perfused for 10 minutes under control conditions and freeze-clamped. Significance of difference from control: [b] $p < 0.05$; [c] $p < 0.01$; [d] $p < 0.001$.

series of experiments did not differ and were therefore grouped together.

Comparison of control values and the values obtained after 2 hours of hypothermic arrest indicated that a significant reduction occurred in aortic output, cardiac output, peak systolic pressure, heart rate, stroke volume, kinetic work, and total work during reperfusion, regardless of the mode of gassing. However, results recorded during reperfusion differed, depending on the composition of the cardioplegic solution and the mode of oxygenation.

Plasmalyte BI

Nonoxygenated Plasmalyte BI caused all hearts to fail, the aortic output being zero (Table 2). This was associated with a significant decline in tissue adenosine triphosphate (ATP) levels measured at the end of the reperfusion period (Table 3).

The variables of mechanical activity measured in hearts having received Plasmalyte BI gassed with 95% O_2/5% CO_2 were significantly higher than those of hearts that received Plasmalyte BI gassed with 100% O_2 during the arrest period. Coronary flow rates were similar, but the aortic and cardiac output, peak systolic pressure, and stroke volume, as well as the work performed (pressure, kinetic, and total), were significantly ($p < 0.001$) lower in the latter group. In fact, 8 of 13 hearts oxygenated with 100% O_2 during cardioplegia failed to produce any aortic output upon reperfusion. Tissue ATP levels of hearts having received Plasmalyte BI gassed with 95% O_2/5% CO_2 were similar to those of control perfused hearts and were also significantly higher than those of hearts that received Plasmalyte BI oxygenated with 100% O_2 (see Table 3).

Plasmalyte BII (high K^+, high Mg^{2+})

Addition of Mg^{2+} (to a final concentration of 16 mmol/L) to the high-K^+ Plasmalyte BI prevented the deleterious effects of oxygenation with 100% O_2: the total work performance of hearts arrested with Plasmalyte BII oxygenated with 95% O_2/5% CO_2 averaged 7.43 ± 0.45 mW compared with 7.89 ± 0.60 mW when oxygenation was done with 100% O_2 (Table 4). Although aortic and cardiac output of hearts that received nonoxygenated Plasmalyte BII were significantly less than those of hearts that received the oxygenated solution, the recovery of these hearts was significantly better than that of hearts that received nonoxygenated Plasmalyte BI (see Table 2). The ATP contents of these three series of hearts were similar (see Table 3).

Plasmalyte BIII (low K^+)

To investigate the possibility that an association of oxygenation with 100% O_2 and high K^+ might be deleterious, the K^+ concentration of the cardioplegic fluid was reduced from 29 to 16 mmol/L. The deleterious effects observed when Plasmalyte BI was gassed with 100% O_2 were completely absent with Plasmalyte BIII: when the K^+ content was lowered to 16 mmol/L, no significant changes were observed between the after-arrest values for 100% O_2 and 95% O_2/5% CO_2 (Table 5). Furthermore, the ATP values were similar in the two series, corresponding to those of control hearts (see Table 3).

Plasmalyte BIV (low K^+, high Mg^{2+})

As observed with the two previous formulations of Plasmalyte B, the mode of oxygenation of Plasmalyte BIV containing low K^+ and high Mg^{2+} (16 mmol/L) levels had no effect on postarrest mechanical recovery (Table 6). In fact, hearts having received nonoxygenated Plasmalyte BIV recovered as well as hearts arrested with 95% O_2/5% CO_2 or 100% O_2 oxygenated Plasmalyte BIV. Furthermore, as was observed with low-K^+ Plasmalyte BIII, the deleterious effects of oxygenation with 100% O_2 were absent. The myocardial ATP contents obtained at the end of the reperfusion period in the three series of hearts were similar to those of the control hearts presented in Table 3.

In summary, the results obtained thus far indicated that the deleterious effects of oxygenation with 100% O_2 were observed only in the presence of high K^+ (29 mmol/L) and low Mg^{2+} (3 mmol/L).

St. Thomas Hospital Solution I

The effects of oxygenation of the conventional formulation of St. Thomas Hospital solution (St. Thomas Hospital

Table 4. Effect of Oxygenation of Plasmalyte BII (high K^+, high Mg^{2+}) on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	18	16.00 ± 0.4	40.00 ± 1.74	46.00 ± 2.03	99 ± 1	269 ± 14	0.21 ± 0.004	12.27 ± 0.46	0.37 ± 0.02	12.64 ± 0.47
Cardioplegia										
Nonoxygenated	6	14.00 ± 1.20	14.50 ± 2.03[d]	28.50 ± 2.71[d]	88 ± 1[d]	315 ± 19	0.09 ± 0.009[d]	5.56 ± 0.55[d]	0.06 ± 0.008[d]	5.61 ± 0.55[d]
95% O_2/5% CO_2	6	13.00 ± 0.45[d]	23.50 ± 1.57[d,f]	36.50 ± 1.97[c,e]	91 ± 1[d]	269 ± 10	0.14 ± 0.008[d,f]	7.32 ± 0.45[d,e]	0.12 ± 0.005[d,g]	7.43 ± 0.45[d,e]
100% O_2	6	13.40 ± 1.27	23.92 ± 1.93[d,f]	37.34 ± 2.55[b,e]	93 ± 1[d,f]	268 ± 22[d]	0.14 ± 0.02[c,e]	7.75 ± 0.58[d,e]	0.14 ± 0.02[d,f]	7.89 ± 0.60[d,e]

[a] Plasmalyte BII contains 29 mmol/L KCl and 16 mmol/L $MgCl_2$. Values are expressed as mean ± standard error of the mean. Significant difference between control and after-arrest values: [b] $p < 0.05$; [c] $p < 0.01$; [d] $p < 0.001$. Significant difference between after-arrest values for nonoxygenated and 95% O_2/5% CO_2 or 100% O_2: [e] $p < 0.05$; [f] $p < 0.01$; [g] $p < 0.001$.

Abbreviations as in Table 2.

Table 5. Effect of Oxygenation of Plasmalyte BIII (low K^+) on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	15	16.00 ± 0.60	42.00 ± 1.00	58.00 ± 1.30	101 ± 1	286 ± 7	0.21 ± 0.08	13.08 ± 0.41	0.34 ± 0.04	13.44 ± 0.43
Cardioplegia										
95% O_2/5% CO_2	8	15.00 ± 1.00	27.00 ± 2.00[c]	42.00 ± 3.50[c]	93 ± 2[b]	289 ± 14	0.16 ± 0.01	8.63 ± 0.80[c]	0.12 ± 0.02[c]	8.75 ± 0.82[c]
100% O_2	7	14.00 ± 0.60	19.00 ± 4.00[c]	33.00 ± 4.00[c]	91 ± 2[b]	262 ± 19	0.11 ± 0.01	6.87 ± 1.01[c]	0.09 ± 0.02[c]	6.95 ± 1.03[c]

[a] Plasmalyte BIII contains 16 mmol/L KCl. No significant changes were observed between after-arrest values for 100% O_2 and 95% O_2/5% CO_2. Significant difference between control and after-arrest values: [b] $p < 0.005$; [c] $p < 0.002$.

Abbreviations as in Table 2.

Table 6. Effect of Oxygenation of Plasmalyte BIV (low K^+, Mg^{2+}) on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	12	14.00 ± 0.05	49.00 ± 1.00	63.00 ± 2.00	105 ± 1	286 ± 9	0.221 ± 0.004	14.69 ± 0.45	0.57 ± 0.05	15.31 ± 0.48
Cardioplegia										
Nonoxygenated	6	13.00 ± 0.70	23.00 ± 2.00[b]	36.00 ± 3.00[b]	93 ± 1[b]	284 ± 15	0.124 ± 0.008[b]	7.32 ± 0.60[b]	0.09 ± 0.01[b]	7.41 ± 0.60[b]
95% O_2/5% CO_2	6	14.50 ± 1.20	27.00 ± 2.00[b]	41.50 ± 2.00[b]	91 ± 1[b]	313 ± 11	0.132 ± 0.006[b]	8.42 ± 0.54[b]	0.15 ± 0.03[b]	8.57 ± 0.56[b]
100% O_2	6	13.00 ± 1.00	29.00 ± 2.00[b]	42.00 ± 2.00[b]	94 ± 2[b]	273 ± 11	0.155 ± 0.009[b]	8.77 ± 0.54[b]	0.17 ± 0.04[b]	8.94 ± 0.57[b]

[a] Plasmalyte BIV contains 16 mmol/L KCl and 16 mmol/L $MgCl_2$. Values are expressed as mean ± standard error of the mean. No significant differences were observed between after-arrest values of nonoxygenated, 95% O_2/5% CO_2, and 100% O_2 oxygenated hearts. [b] $p < 0.001$ versus control.

Abbreviations as in Table 2.

Table 7. Effect of Oxygenation of St. Thomas Hospital Solution I on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	7	15.93 ± 1.03	44.50 ± 2.88	60.35 ± 2.94	103 ± 2	267 ± 13	0.228 ± 0.012	13.85 ± 0.94	0.62 ± 0.14	14.47 ± 1.07
Cardioplegia										
Nonoxygenated	6	13.50 ± 0.98	29.33 ± 3.96[c]	46.70 ± 5.70[b]	95 ± 2[c]	269 ± 31	0.173 ± 0.009[d]	9.08 ± 1.16[c]	0.22 ± 0.06[b]	9.29 ± 1.21[c]
95% O_2/5% CO_2	6	12.40 ± 0.60[c]	28.63 ± 2.38[d]	41.02 ± 2.77[d]	92 ± 2[d]	271 ± 12	0.155 ± 0.016[d]	8.29 ± 0.71[d]	0.16 ± 0.04[c]	8.44 ± 0.75[d]
100% O_2	6	17.00 ± 0.80	25.00 ± 4.00[d]	42.00 ± 5.00[c]	97 ± 2	290 ± 14	0.200 ± 0[b]	9.40 ± 1.30[c]	0.10 ± 0.0[d]	9.50 ± 1.30[c]

[a] Results are expressed as mean ± standard error of the mean. Significant difference versus control: [b] $p < 0.05$; [c] $p < 0.02$; [d] $p < 0.005$.

Abbreviations as in Table 2.

solution I) on mechanical recovery after 2 hours of hypothermic arrest were similar to those observed with Plasmalyte BIV: hearts receiving nonoxygenated St. Thomas Hospital solution recovered to the same extent as those having received oxygenated cardioplegia (Table 7). Furthermore, the mode of oxygenation (95% O_2/5% CO_2 and 100% O_2) had no effect on the outcome of the results, and hearts in both series recovered equally well. As was observed before, the high-energy phosphate contents were similar in all three series and comparable with those of control hearts (see Table 3).

St. Thomas Hospital Solution II

The results obtained thus far indicated that oxygen toxicity could only be demonstrated in hearts having received Plasmalyte B containing high K^+ levels (29 mmol/L) (see Table 2). To determine whether these high K^+ levels per se were responsible for the changes observed, the K^+ content of the St. Thomas Hospital solution was elevated to 29 mmol/L and its effects were studied under similar experimental conditions. The results obtained indicated that hearts arrested with high-K^+ St. Thomas Hospital solution II oxygenated with either 95% O_2/5% CO_2 or 100% O_2 recovered equally well when reperfused (Table 8). The ATP content of these two series of hearts was similar (see Table 3).

St. Thomas Hospital Solution III

To determine whether the combination of high K^+ and low Mg^{2+} (cf, Plasmalyte BI) predisposes towards oxygen toxicity, the previous experiment was repeated using St. Thomas Hospital solution containing 29 mmol/L K^+ and 3 mmol/L Mg^{2+}. Although mechanical recovery of hearts arrested with St. Thomas Hospital solution III oxygenated with 95% O_2/5% CO_2 was significantly higher than that of hearts receiving cardioplegic fluid gassed with 100% O_2, recovery of the latter group was similar to that observed with St. Thomas Hospital solution II (Table 9).

St. Thomas Hospital Solution IV

In this series the role of HCO_3^-, the only remaining major difference between Plasmalyte BI and St. Thomas Hospital solution I, was addressed. By modifying St. Thomas Hospital solution to contain high K^+ (29 mmol/L), low Mg^{2+} (3 mmol/L), and high HCO_3^- (28 mmol/L) levels, the results obtained showed similar tendencies as those observed with Plasmalyte BI: the mechanical recovery as well as ATP contents of hearts arrested with either nonoxygenated or St. Thomas Hospital solution IV oxygenated with 100% O_2 were significantly lower than those of hearts having received St. Thomas Hospital solution IV gassed with 95% O_2/5% CO_2 (Table 10).

Effect of Oxygenation on Tissue Ca^{2+} After 2 Hours of Hypothermic Cardioplegic Arrest and Reperfusion

To determine whether the reduction in mechanical activity during reperfusion after arrest with Plasmalyte BI and St. Thomas Hospital solution IV (gassed with 100% O_2) was associated with intracellular Ca^{2+} overloading, tissue Ca^{2+} levels were determined in a limited number of studies: after arrest with Plasmalyte BI and St. Thomas Hospital solutions II and IV. The results showed that oxygenation with 100% O_2 of Plasmalyte BI and St. Thomas Hospital solution IV caused a significant ($p < 0.02$) increase in tissue Ca^{2+} content when compared with those of hearts having received the same solutions gassed with 95% O_2/5% CO_2 (Table 11). In the case of St. Thomas Hospital solution II, where the mode of oxygenation did not affect mechanical recovery during reperfusion, no differences were observed between tissue Ca^{2+} content of hearts arrested with the cardioplegic fluid gassed with 100% O_2 or 95% O_2/5% CO_2.

Effect of Oxygenation on pH and Gas Tensions of Cardioplegic Solutions

The pH of nonoxygenated Plasmalyte BI, Plasmalyte BIII, and the different formulations of St. Thomas Hospital solution averaged 7.40, 7.50 and 7.80, respectively (Table 12). Oxygenation with 100% O_2 caused a rapid increase in the pH of all solutions, reaching values greater than 8 within 5 minutes. After 2 hours of continuous gassing with 100% O_2, pH values of 8.65 and 8.81 were obtained with Plasmalyte BI and BIII, respectively. Similar high pH values were observed with St. Thomas Hospital solution, exceeding 9 in the case of solution IV. On the other hand, gassing with 95% O_2/5% CO_2 for 2 hours reduced pH values to less than 7.4.

The partial pressures of oxygen and carbon dioxide were also monitored at different time intervals (measurements were made at 37°C). The mean values obtained over a 2-hour period are summarized in Table 12. The oxygen tensions of the ungassed cardioplegic solutions were similar, averaging 198 mm Hg. Gassing with either 100% O_2 or 95% O_2/5% CO_2 caused an immediate increase in oxygen tension; values ranging between 450 and 500 mm Hg were maintained.

The carbon dioxide tension values of ungassed Plasmalyte BI, Plasmalyte BIII, and the St. Thomas Hospital solution averaged 31, 22, and 4.4 mm Hg, respectively. In all solutions the carbon dioxide tension was reduced to 1.2 to 2.2 mm Hg throughout the cardioplegic period when gassed with 100% O_2. On the other hand, the carbon dioxide tension of the solutions was increased to 39 to 50 mm Hg when oxygenated with 95% O_2/5% CO_2.

Comment

Previous results from our laboratory demonstrated the oxygen dependence of the hypothermic arrested rat heart: substantial amounts of oxygen are consumed at a relatively constant rate over at least 5 hours [3]. A basal metabolic requirement of approximately 0.3 mL $O_2 \cdot 100\ g^{-1} \cdot min^{-1}$ was also reported for the cardioplegia-arrested dog heart [12]. It is therefore not surprising that oxygenation of crystalloid cardioplegic solutions (eg, Plasmalyte B and St. Thomas Hospital solution) markedly improves metabolic and mechanical recovery during reperfusion [2–4].

However, in view of the fact that 95% O_2/5% CO_2 and 100% O_2 were used for oxygenation of Plasmalyte B and

Table 8. Effect of Oxygenation of St. Thomas Hospital Solution II on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_p (mW)	W_k (mW)	W_{Total} (mW)
Control	6	16.80 ± 1.04	39.00 ± 1.91	56.20 ± 2.66	94 ± 1	295 ± 14	0.191 ± 0.009	11.66 ± 0.62	0.26 ± 0.003	11.92 ± 0.66
Cardioplegia										
95% O_2/5% CO_2	6	18.50 ± 2.89	13.90 ± 1.40^{c}	32.40 ± 2.81^{c}	88 ± 1^{b}	307 ± 11	0.110 ± 0.001^{c}	6.39 ± 0.61^{c}	0.06 ± 0.001^{c}	6.45 ± 0.62^{c}
100% O_2	6	18.30 ± 2.45	14.10 ± 1.04^{c}	32.20 ± 2.28^{c}	91 ± 3^{b}	288 ± 35	0.130 ± 0.002^{c}	6.49 ± 0.52^{c}	0.10 ± 0.002^{c}	6.58 ± 0.54^{c}

[a] St. Thomas Hospital Solution II contains 29 mmol/L KCl and 16 mmol/L $MgCl_2$. Results are expressed as mean ± standard error of the mean. Significant difference between control and after-arrest values: [b] $p < 0.01$; [c] $p < 0.001$.

Abbreviations as in Table 2.

Table 9. Effect of Oxygenation of St. Thomas Hospital Solution III on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_P (mW)	W_k (mW)	W_{Total} (mW)
Control	6	16.33 ± 0.56	43.00 ± 1.32	59.33 ± 1.54	102 ± 1	281 ± 7	0.210 ± 0.006	13.42 ± 0.39	0.29 ± 0.03	13.71 ± 0.41
Cardioplegia										
95% O_2/5% CO_2	6	16.00 ± 0.82	34.70 ± 1.96^{b}	50.70 ± 2.56	96 ± 1^{c}	306 ± 15	0.170 ± 0.006^{c}	10.82 ± 0.56^{b}	0.21 ± 0.03	11.02 ± 0.59^{b}
100% O_2	6	15.17 ± 0.46	21.00 ± 2.24^{c,f}	36.17 ± 2.47^{c,e}	92 ± 1^{c}	301 ± 13	0.130 ± 0.01^{c,e}	7.35 ± 0.59^{c,e}	0.11 ± 0.02^{c,d}	7.47 ± 0.60^{c,e}

[a] St. Thomas Hospital Solution III contains 29 mmol/L KCl and 3 mmol/L $MgCl_2$. Results are expressed as mean ± standard error of the mean. Significant difference between control and after-arrest values: [b] $p < 0.01$; [c] $p < 0.001$. Significant difference between after-arrest values for 95% O_2/5% CO_2 and 100% O_2: [d] $p < 0.05$; [e] $p < 0.01$; [f] $p < 0.001$.

Abbreviations as in Table 2.

Table 10. Effect of Oxygenation of St. Thomas Hospital Solution IV on Cardiac Function During Reperfusion After 2 Hours' Arrest at 20°C[a]

Group	n	Coronary Flow (mL/min)	Aortic Output (mL/min)	Cardiac Output (mL/min)	PSP (mm Hg)	HR (beats/min)	SV (mL/beat)	W_P (mW)	W_k (mW)	W_{Total} (mW)
Control	6	16.80 ± 0.49	41.40 ± 2.38	58.20 ± 2.58	101 ± 2	302 ± 8	0.190 ± 0.007	13.05 ± 0.75	0.33 ± 0.06	13.38 ± 0.81
Cardioplegia										
Nonoxygenated	6	13.20 ± 1.78	9.44 ± 0.70^{c}	22.60 ± 2.04^{c}	89 ± 1^{b}	306 ± 18	0.074 ± 0.005^{c}	4.46 ± 0.38^{c}	0.06 ± 0.02^{c}	4.57 ± 0.40^{c}
95% O_2/5% CO_2	6	15.00 ± 0.71	25.20 ± 2.24^{c}	40.20 ± 2.22^{c}	93 ± 1^{b}	286 ± 9	0.140 ± 0.01^{b}	8.29 ± 0.55^{c}	0.10 ± 0.01^{b}	8.37 ± 0.58^{c}
100% O_2	12	12.86 ± 0.68^{c}	6.75 ± 1.69^{c,d}	19.75 ± 2.00^{c,d}	83 ± 2^{c,d}	281 ± 10	0.070 ± 0.005^{c,d}	3.84 ± 0.42^{c,d}	0.03 ± 0.005^{c,d}	3.86 ± 0.42^{c,d}

[a] St. Thomas Hospital Solution IV contains 29 mmol/L KCl, 3 mmol/L $MgCl_2$, and 28 mmol/L $NaHCO_3$. Results are expressed as mean ± standard error of the mean. Significant difference between control and after-arrest values: [b] $p < 0.01$; [c] $p < 0.001$. Significant difference between after-arrest values for 95% O_2/5% CO_2 and 100% O_2: [d] $p < 0.001$.

Abbreviations as in Table 2.

Table 11. Tissue Ca^{2+} Contents After 2 Hours of Hypothermic Cardioplegic Arrest and Reperfusion: Effects of Composition and Mode of Oxygenation of Cardioplegic Solution

Cardioplegic Solution	n	Tissue Ca^{2+} (μmol/g dry weight)	p Value
Plasmalyte BI			<0.02
95% O_2/5% CO_2	6	5.93 ± 0.14	
100% O_2	5	7.57 ± 0.55	
St. Thomas Solution II			Not significant
95% O_2/5% CO_2	6	5.16 ± 0.19	
100% O_2	6	5.46 ± 0.28	
St. Thomas Solution IV			<0.02
95% O_2/5% CO_2	6	5.67 ± 0.32	
100% O_2	6	8.17 ± 0.74	

St. Thomas Hospital solution, respectively, which in turn caused marked pH differences, we were prompted to reevaluate the mode of oxygenation. The results summarized in Table 2 confirm our previous observations that oxygenation of Plasmalyte BI with 95% O_2/5% CO_2 significantly improved myocardial functional and metabolic (as evidenced by tissue ATP levels) recovery, whereas hearts receiving nonoxygenated cardioplegic fluid showed signs of failure within 90 minutes (unpublished observations). However, oxygenation of Plasmalyte BI with 100% O_2 caused a significant depression in mechanical recovery and tissue ATP levels (see Tables 2, 3) (8 out of 13 hearts failed to produce aortic output in this series).

In marked contrast to these findings, oxygenation did not prove to be essential for recovery of hearts arrested by the conventional St. Thomas Hospital solution I (the beneficial effects of oxygenation of this cardioplegic solution become evident only after 4 hours of hypothermic arrest) [4]. Furthermore, the mode of oxygenation was not relevant: hearts having received St. Thomas Hospital solution I gassed with either 100% O_2 or 95% O_2/5% CO_2 recovered equally well when reperfused (see Table 7).

Comparison of the ionic compositions of Plasmalyte BI and St. Thomas Hospital solution I (see Table 1) showed major differences in KCl, $MgCl_2$, and $NaHCO_3$ contents. Manipulation of the composition of Plasmalyte BI (Tables 2, 4–6), showed that oxygenation with 100% O_2 only becomes deleterious at one specific formulation of Plasmalyte B: 29 mmol/L KCl, 3 mmol/L $MgCl_2$, and 28 mmol/L $NaHCO_3$. Increasing the $MgCl_2$ concentration (Plasmalyte BII) or lowering the KCl concentration (Plasmalyte BIII) to 16 mmol/L each, as well as a combination of these changes (Plasmalyte BIV), effectively prevented the harmful effects of 100% O_2. Furthermore, with these formulations oxygenation no longer becomes a prerequisite for mechanical and metabolic recovery after 2 hours of hypothermic arrest. These conclusions were confirmed by introducing the same ionic changes in St. Thomas Hospital solution. Mere elevation of the KCl concentration to 29 mmol/L or lowering of the $MgCl_2$ to 3 mmol/L while maintaining the $NaHCO_3$ concentration at 10 mmol/L did not exhibit the deleterious effects of oxygenation with 100% O_2 (see Tables 7–10).

Table 12. Effects of Oxygenation on pH and Gas Tensions of Cardioplegic Solutions[a]

Group	pH				Oxygen Tension (mm Hg)	Carbon Dioxide Tension (mm Hg)
	0 min	5 min	30 min	120 min		
Plasmalyte BI						
100% O_2	7.40	8.05	8.55	8.65	495	1.2
95% O_2/5% CO_2		7.45	7.30	7.28	462	43
Plasmalyte BIII						
100% O_2	7.50	8.05	8.50	8.81	452	1.2
95% O_2/5% CO_2		7.45	7.36	7.33	451	45
St. Thomas Hospital solution I						
100% O_2	7.78	8.09	8.29	8.76	488	1.1
95% O_2/5% CO_2		7.04	7.00	7.00	458	44
St. Thomas Hospital solution II						
100% O_2	7.79	8.10	8.12	8.42	488	2.2
95% O_2/5% CO_2		7.11	7.06	7.30	451	39
St. Thomas Hospital solution III						
100% O_2	7.80	8.23	8.40	8.83	468	1.8
95% O_2/5% CO_2		7.00	7.00	7.10	451	44
St. Thomas Hospital solution IV						
100% O_2	7.80	8.29	8.48	9.01	456	1.6
95% O_2/5% CO_2		7.28	7.25	7.32	471	50

[a] All measurements were made at 37°C. Gas tensions represent mean values obtained over a 2-hour period.

Because oxygenation with 95% O_2/5% CO_2 of Plasmalyte BI and St. Thomas Hospital solution IV had no harmful effects on the mechanical and metabolic recovery of the arrested heart, it was concluded that, in addition to the above-mentioned ionic composition, an alkalotic pH (greater than 8) was essential to elicit the detrimental effects of oxygenation with 100% O_2. These deleterious effects were also evident at a cellular level as shown by the reduction in ATP levels and intracellular Ca^{2+} overloading in these hearts (see Tables 3, 11). An explanation for these findings is not readily available, and several factors should be considered.

Effects of K^+ and Mg^{2+}

A K^+ concentration of 29 mmol/L per se should be disregarded as a possible causal factor, because oxygenation of Plasmalyte BI with 95% O_2/5% CO_2 improved both functional and metabolic recovery. Furthermore, although a K^+ concentration of 15 to 16 mmol/L was found to yield good protection [13, 14], concentrations of up to 240 mmol/L have been reported to be relatively safe [15].

Similarly, although Mg^{2+} exerts, in a complex dose-related manner, a marked protection on the ischemic rat heart [16], it is unlikely that the low concentration of this ion (3 mmol/L) per se is responsible for the toxic effects of 100% O_2.

Effects of pH

Oxygenation of a bicarbonate solution will alter the partial pressure of CO_2 in the solution, thereby affecting the relationship between HCO_3^-/CO_2 [17] and causing a change in pH. Oxygenation with 100% O_2 of all formulations of Plasmalyte B and St. Thomas Hospital solution caused a "washout" of CO_2 from the crystalloid solutions (carbon dioxide tension, 1 to 2 mm Hg) concomitant with an immediate increase in pH (values greater than 8 were observed within minutes) (see Table 12). Although previous studies suggested that a relatively acidotic cardioplegic solution (pH 7.0 to 7.1) improved myocardial function after hypothermic arrest [18, Von Oppell UO, et al, unpublished results] several observations indicate that a cardioplegic solution with a high pH is not necessarily detrimental to the heart: (1) Plasmalyte BII, BIII, and BIV, as well as St. Thomas Hospital solution I, II, and III, whether oxygenated with 100% O_2 (pH greater than 8) or oxygenated with 95% O_2/5% CO_2 (pH 7.1 to 7.32), yielded similar functional and metabolic recoveries (see Tables 4–9). (2) Cardioplegic solutions with a pH of 7.8 to counteract acidosis have been reported to be effective cardioprotectants at 27°C [19]. Follette and co-workers [20] reported that increasing the pH of a hypocalcemic, hyperkalemic reperfusate to 7.8 resulted in improved recovery.

Ionic Interactions

Because none of the variables (KCl, $MgCl_2$, $NaHCO_3$, and pH) per se appeared to be responsible for the deleterious effects of 100% O_2, possible complex ionic interactions occurring in a high K^+-low Mg^{2+}-high $NaHCO_3$ alkalotic solution should be considered. There is evidence for more than one mechanism. For example, Del Nido and coworkers [19] observed that although a combination of high extracellular K^+ and high pH levels preserved myocardial ATP, it caused substantial reperfusion necrosis. It is also known that alkalinization potentiates lactate production, which in turn has adverse effects on cardiovascular function [21]. An early study by Hearse and coworkers [16] suggested a complex interaction between Mg^{2+} and Na^+ ions, which markedly affected the myocardial recovery potential; mechanical recovery of hearts arrested with a low Mg^{2+}-high Na^+ cardioplegic solution was significantly lower than that of hearts having received high Mg^{2+}-lower Na^+ (56.5% and 90.6% of control, respectively).

In view of the established relationship between myocardial ATP levels and functional recovery during reperfusion [2, 3], it is suggested that mechanical failure of these hearts is caused by the significant reduction in ATP content (see Table 3). The latter phenomenon is probably due to the increased intracellular Ca^{2+}, which is known to affect mitochondrial oxidative phosphorylation and ATP production [22]. However, the exact mechanism whereby the above formulation caused intracellular Ca^{2+} overloading and a reduction in myocardial ATP levels remains to be established. Possibilities to be considered are: (1) influx of excess Ca^{2+} due to depolarization of the sarcolemma by high extracellular K^+; (2) potentiation by high K^+ and an alkalotic pH of the effects of a suboptimal Mg^{2+}/Na^+ ratio; and (3) production of hydroxyl radicals by oxygenation of an alkalotic solution which, in turn, may cause membrane damage and calcium overloading [23].

Finally, the results obtained in this study again stress the importance of adequate laboratory testing of cardioplegic solutions. Nonoxygenated Plasmalyte BI has been used successfully in clinical practice for many years, underlining Buckberg's [24] remark that extrapolation of experimental results to the intact human should be done with care because of noncoronary collateral flow, which reduces the harmful effects of improperly designed solutions. St. Thomas Hospital solution I is clearly superior to Plasmalyte BI, particularly under nonoxygenated conditions.

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References

1. Bodenhamer RM, DeBoer LWV, Geffin GA, et al. Enhanced myocardial protection during ischemic arrest. Oxygenation of a crystalloid solution. J Thorac Cardiovasc Surg 1983;86:769–80.
2. Coetzee A, Kotze J, Louw J, Lochner A. Effect of oxygenated crystalloid cardioplegia on the functional and metabolic recovery of the isolated perfused rat heart. J Thorac Cardiovasc Surg 1986;91:259–69.
3. De Wit L, Coetzee A, Kotze J, Lochner A. Oxygen requirements of the isolated rat heart during hypothermic cardioplegia. J Thorac Cardiovasc Surg 1988;95:310–20.
4. Ledingham SJM, Braimbridge MV, Hearse DJ. Improved myocardial protection by oxygenation of the St Thomas

Hospital cardioplegic solutions. J Thorac Cardiovasc Surg 1988;95:103–11.

5. Ledingham SJM, Braimbridge MV, Hearse DJ. The St Thomas Hospital cardioplegic solution. A comparison of the efficacy of two formulations. J Thorac Cardiovasc Surg 1987; 93:240–6.
6. Neely JR, Liebermeister H, Battersby EJ, Morgan HE. Effects of pressure development on oxygen consumption by isolated rat hearts. Am J Physiol 1967;212:804–14.
7. Opie LH, Mansford KRL, Owen P. Effect of increased heart work on glycolysis and adenine nucleotide in the perfused heart of normal and diabetic rats. Biochem J 1971;124:475–90.
8. Kannengieser GJ, Opie LH, Van der Werff TJ. Impaired cardiac work and oxygen uptake after reperfusion of regionally ischemic myocardium. J Mol Cell Cardiol 1979;11: 197–207.
9. Gutman I, Wahlefeld A. In: Bergmeyer HU, ed. Methods in enzymatic analysis. New York: Academic Press, 1963:146.
10. Victor T, Jordaan AM, Bester AJ, Lochner A. A sensitive and rapid method for separating adenine nucleotides and creatinine phosphate by ion-pair reversed-phase high-performance liquid chromatography. J Chromatogr 1987;389: 339–44.
11. Nayler WG, Perry SE, Elz JS, Daly MJ. Calcium, sodium and the calcium paradox. Circ Res 1984;55:227–37.
12. Buckberg GD, Brazier JR, Nelson RL, Goldstein SM, McConnel DH, Cooper N. Studies of the effects of hypothermia on regional myocardial blood flow and metabolism during cardiopulmonary bypass. 1. The adequately perfused beating, fibrillating and arrested heart. J Thorac Cardiovasc Surg 1977;73:87–94.
13. Ledingham SJM, Braimbridge MV, Hearse DJ. The St Thomas' Hospital cardioplegic solution. A comparison of the efficacy of two formulations. J Thorac Cardiovasc Surg 1987; 93:240–6.
14. Engelman RM, Auvil J, O'Donoghue MJ, Levitsky S. The significance of multidose cardioplegia and hypothermia in myocardial preservation during ischemic arrest. J Thorac Cardiovasc Surg 1978;75:555–63.
15. Jellinek M, Standeven JW, Menz LJ, Hahn JW, Barner HB. Cold blood potassium cardioplegia. Effects of increasing concentrations of potassium. J Thorac Cardiovasc Surg 1981; 82:26–37.
16. Hearse DJ, Stewart DA, Braimbridge MV. Myocardial protection during ischemic cardiac arrest. The importance of magnesium in cardioplegic infusates. J Thorac Cardiovasc Surg 1978;75:877–85.
17. West JB. Respiratory physiology. The essentials. 3rd ed. Baltimore: Williams & Wilkens, 1985:67–83.
18. Nugent WC, Levine FH, Liatis CD, LaRaia PJ, Tsai CH, Buckley M. Effects of the pH of cardioplegic solution on postarrest myocardial preservation. Circulation 1982;66: 158–72.
19. Del Nido P, Wilson GJ, Mickle DAG, et al. The role of cardioplegic solution buffering in myocardial protection. J Thorac Cardiovasc Surg 1985;89:689–99.
20. Follette DM, Fey K, Buckberg GD, et al. Reducing postischemic damage by temporary modification of reperfusate calcium, potassium, pH and osmolarity. J Thorac Cardiovasc Surg 1981;82:221–38.
21. Hindman BJ. Sodium bicarbonate in the treatment of subtypes of acute lactic acidosis: physiologic considerations. Anesthesiology 1990;72:1064–76.
22. Nakanishi T, Nishioka K, Jarmakani JM. Mechanism of tissue Ca^{2+} gain during reoxygenation after hypoxia in rabbit myocardium. Am J Physiol 1982;242:H437–49.
23. Kaneko M, Beamish RE, Dhalla NS. Depression of heart sarcolemmal Ca^{2+}-pump activity by oxygen free radicals. Am J Physiol 1989;256:H368–74.
24. Buckberg GD. A proposed "solution" to the cardioplegic controversy. J Thorac Cardiovasc Surg 1979;77:803–15.

Production of Endothelium-Derived Contracting Factor Is Enhanced After Coronary Reperfusion

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To determine whether coronary reperfusion enhances the production of endothelium-derived contracting factor, we investigated dogs subjected to global cardiac ischemia (45 minutes) followed by reperfusion (60 minutes). Segments of reperfused and control coronary arteries were suspended in organ chambers to measure isometric force. Perfusate hypoxia caused endothelium-dependent contraction in the control and reperfused arteries. However, reperfused arteries exhibited hypoxic contraction that was significantly greater than control segments. The hypoxic contractions in both the control and reperfused arteries could be inhibited by N^G-monomethyl-L-arginine (L-NMMA), the blocker of endothelial cell synthesis of nitric oxide from L-arginine. The action of L-NMMA could be reversed by L-arginine but not D-arginine. Thus, after reperfusion, augmented production of endothelium-derived contracting factor occurs by an L-arginine–dependent pathway. We hypothesize that nitric oxide produced by L-arginine metabolism combines with superoxide anion to produce the peroxynitrite anion ($ONOO^-$), which is metabolized to endothelium-derived contracting factor or induces its synthesis. Augmented production of endothelium-derived contracting factor would favor vasospasm after reperfusion.

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The coronary endothelium modulates vascular tone and myocardial perfusion by producing vasoactive factors that act on the underlying vascular smooth muscle [1]. However, after global cardiac ischemia and reperfusion, the release of endothelium-derived relaxing factor to aggregating platelets and platelet products becomes impaired [2, 3]. Impaired release of relaxing factor would promote platelet adhesion and aggregation as well as platelet-induced constriction of the coronary smooth muscle; these events would be expected to increase risk of subsequent ischemia due to vasospasm and thrombosis [4]. Indeed, impaired release of endothelium-dependent relaxing factor, in particular to aggregating platelets, appears to be an important cause of coronary vasospasm after cardiac operations.

The coronary endothelium can also produce contracting factor (EDCF). When exposed to hypoxia, coronary segments with endothelium exhibit augmented contraction to agonists such as serotonin, prostaglandin $F_{2\alpha}$, and potassium ions [5, 6]. Endothelium-dependent contractions caused by hypoxia have also been described in the human internal mammary artery [7].

It is possible that coronary reperfusion could enhance the production of EDCF. Increased production of EDCF after global myocardial reperfusion as occurs during cardiopulmonary bypass might lead to coronary vasospasm after cardiac operations. The present study was designed to determine whether reperfusion after cardiopulmonary bypass alters the production of EDCF.

Material and Methods

Animal Preparation

Heartworm-free mongrel dogs (25 to 30 kg) of either sex were anesthetized with intravenous pentobarbital sodium (30 mg/kg bolus injection; Fort Dodge Laboratories, Fort Dodge, IA), intubated with a cuffed endotracheal tube, and ventilated with 95% oxygen. The left common carotid artery was isolated and catheterized to monitor aortic blood pressure. A left lateral thoracotomy was performed in the fourth intercostal space to expose the heart, and a pericardial cradle was created. After heparinization (2 mg/kg), the right atrium was cannulated through its appendage for venous return, and the right femoral artery was isolated and cannulated for arterial inflow. Cardiopulmonary bypass was then commenced at 2.0 to 2.4 $L \cdot min^{-1} \cdot m^{-2}$ (32°C). When perfusion flow and pressure were stable, the ascending aorta was cross-clamped. A left ventricular vent was then inserted through the left atrial appendage to decompress the heart during ischemia and reperfusion. After 45 minutes of normothermic arrest, the aortic cross-clamp was removed, and the heart was allowed to reperfuse. After 5 minutes of reperfusion, the heart was defibrillated, and cardiopulmonary bypass was slowly discontinued. The heart was then allowed to function for a total of 60 minutes of reperfusion, at which time the animal was exsanguinated into the cardiotomy reservoir, and the still-beating heart was excised and immersed in cold, oxygenated physiological salt solution of the following composition (mmol/L): NaCl, 118.3; KCl, 4.7; $MgSO_4$, 1.2; KH_2PO_4, 1.22; $CaCl_2$, 2.5; $NaHCO_3$, 25.0, and glucose, 11.1 (control solution). An additional dog was anesthetized (sodium pentobarbital, 30 mg/kg intravenous injection) and exsanguinated, and the beating

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heart excised and placed in cold, oxygenated control solution. Preliminary experiments demonstrated no difference in the hypoxic response between exsanguinated control dogs and dogs exposed to cardiopulmonary bypass without ischemia (data not shown). All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). The procedures and the handling of the animals were reviewed and approved by the Institutional Animal Care and Use Committee of the Mayo Foundation.

In Vitro Experiments

The left circumflex arteries of reperfused and unmanipulated control hearts were carefully dissected free and placed in control solution. Care was taken to remove as much of the connective tissue as possible. A maximum of four coronary ring segments (5 to 6 mm in length) were prepared from each artery. In some rings, the endothelium was removed by gently rubbing the intimal surface with the tip of a pair of watchmaker's forceps [8, 9]. Previous histological studies have shown that this procedure removes the endothelial cells in large canine arteries and preserves the ability of the vascular smooth muscle to contract and relax [10, 11].

The rings were suspended in 25-mL organ chambers filled with control solution maintained at 37°C and aerated with 95% O_2–5% CO_2 (pH = 7.4) (Fig 1). Each ring was suspended by two stainless steel clips passed through the lumen. One clip was anchored to the bottom of the organ chamber; the other was connected to a strain gauge (Grass FT03; Grass Instrument Co, Quincy, MA) for the measurement of isometric force. Rings were placed at the optimal point of their length-tension relationship by progressively stretching them until the contraction to KCl (20 mmol/L), imposed at each level of distention, was maximal [8, 9]. In all experiments, the presence or absence of endothelium was confirmed by the response to acetylcholine (10^{-6} mol/L) of rings contracted with potassium ions (20 mmol/L) [10, 12]. After optimal tension was achieved, the rings were allowed to equilibrate for 45 minutes before the administration of drugs.

Protocols

Rings of reperfused and control arteries (with and without endothelium) were studied in parallel. Before exposure to hypoxia, rings were contracted with prostaglandin $F_{2\alpha}$ so that the vessel could either relax or exhibit additional contraction to hypoxia [5, 13]. Previous experiments have shown that control and reperfused canine coronary arteries exhibit the same contractile response to prostaglandin $F_{2\alpha}$ [2]. Reperfused coronary segments also exhibit normal active basal tone as evidenced by relaxations to nitric oxide and isoproterenol [2]. Hypoxia was induced by aerating the organ bath with a mixture of 95% N_2–5% CO_2 (pH = 7.4, oxygen tension = 30 to 40 mm Hg, 20 min). Rings were only exposed to one period of hypoxia. When used to modify the hypoxic response, drugs were added to the organ chamber at least 10 minutes before the addition of the prostaglandin $F_{2\alpha}$.

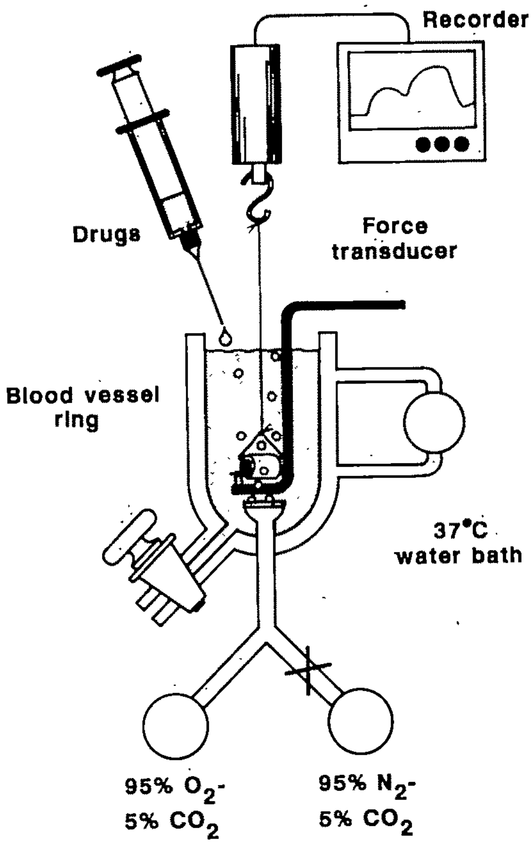


Fig 1. Organ chamber for the in vitro study of isolated blood vessels.

Drugs

The following drugs were used: acetylcholine chloride (Sigma Chemical Co, St. Louis, MO), KCl (Sigma), D-arginine (Calbiochem, San Diego, CA), L-arginine (Calbiochem), N^G-monomethyl-L-arginine acetate (Calbiochem), and prostaglandin $F_{2\alpha}$ (Sigma). The concentrations are expressed as final molar concentration in the organ chamber.

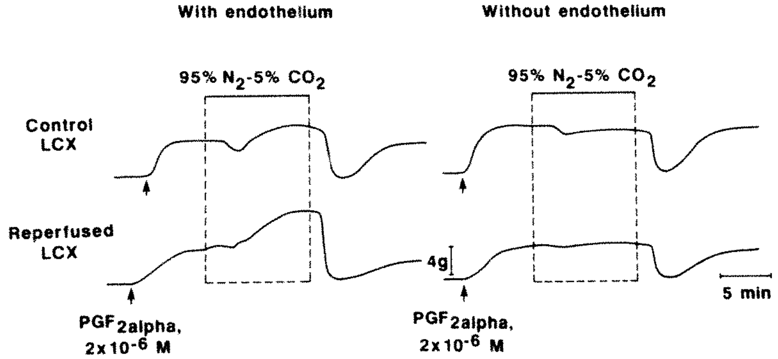
Data Analysis

The results are expressed as mean ± standard error of the mean. In all experiments, n refers to the number of animals from which rings were taken. In rings contracted with prostaglandin $F_{2\alpha}$, responses are expressed as percent change from the contracted levels. Statistical evaluation of the data was performed by Student's *t* test for either paired or unpaired observations. Values were considered to be statistically significant when p was smaller than 0.05.

Results

Control and reperfused coronary segments with and without endothelium exhibited comparable contractile response to prostaglandin $F_{2\alpha}$ (2×10^{-6} mol/L): 6.05 ±

Fig 2. Isometric tension recording of the effect of global myocardial ischemia and reperfusion on endothelium-dependent responses to hypoxia. Dogs were subjected to global myocardial ischemia (45 minutes) followed by reperfusion (60 minutes). Segments from control and reperfused arteries were suspended in organ chambers and contracted with prostaglandin $F_{2\alpha}$ ($PGF_{2\ alpha}$)(2×10^{-6} mmol/L). When the contractile response to $PGF_{2\alpha}$ was stable, hypoxia was induced by changing to a 95% N_2–5%CO_2 gas mix. (LCX = left circumflex coronary artery.)



0.82 and 5.00 ± 0.51 g for control and reperfused arteries with endothelium, and 6.47 ± 0.83 and 6.70 ± 0.83 g for control and reperfused arteries without endothelium (n = 6). In contracted control and reperfused coronary segments, hypoxia caused an initial decrease in tension in segments with and without endothelium (hypoxic inhibition) (Figs 2, 3); this transient decrease in tension was comparable in the control and reperfused arteries. Hypoxia then induced contraction in control and reperfused segments with endothelium (hypoxic potentiation) (Figs 2, 3). The hypoxic contraction of the reperfused coronary segments was significantly greater than that of control coronary segments (168.0% ± 20.1% versus 117.7% ± 17.2% of initial prehypoxic tension, respectively; n = 6; $p < 0.05$). Reoxygenation produced comparable transient relaxations in control and reperfused segments with and without endothelium (posthypoxic inhibition). Coronary segments then gradually returned to their original prehypoxia tension (posthypoxic recovery).

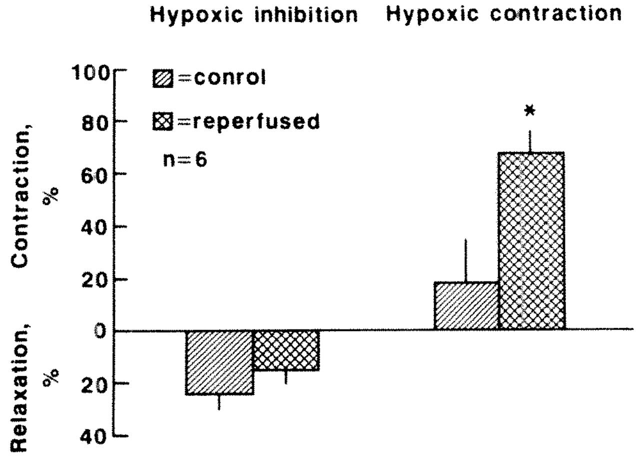


Fig 3. Effect of hypoxia (95% N_2–5% CO_2) on tension in contracted (prostaglandin $F_{2\alpha}$, 2×10^{-6} M) control and reperfused canine coronary segments with endothelium. Data are shown as mean ± standard error of the mean (n = 6) and expressed as percent of the initial contraction to prostaglandin. (Hypoxic inhibition = *initial transient dilation exhibited by the coronary segment when exposed to hypoxia;* hypoxic contraction = *subsequent endothelium-dependent constriction exhibited by the coronary artery segment when exposed to hypoxia;* asterisk *denotes significant difference from control segments with endothelium* [$p < 0.05$].)

Pretreatment of control and reperfused coronary segments with N^G-monomethyl-L-arginine (L-NMMA) (10^{-5} mol/L) inhibited the hypoxic contractions in the coronary segments with endothelium but had no effect on segments without endothelium (n = 5; $p < 0.05$) (Figs 4, 5). The effect of L-NMMA could be blocked with L-arginine (10^{-4} mol/L) but not by D-arginine (10^{-4} mol/L) (Figs 4, 5). L-arginine and D-arginine had no effect on the hypoxic response of control and reperfused segments without endothelium.

Comment

The major finding of this study is that early after global ischemia and reperfusion, hypoxia induces augmented endothelium-dependent contraction in the epicardial coronary artery. In addition, we determined that hypoxic contraction is mediated by an L-arginine–dependent pathway.

Release of endothelium-derived relaxing factor (EDRF) in the coronary artery, particularly the release induced by aggregating platelets, is impaired early after global myocardial ischemia and reperfusion during cardiopulmonary bypass [2], and early and late after regional myocardial ischemia [8, 9]. Because EDRF induces vasodilation [12], inhibits platelet adhesion [14] and aggregation [15, 16], and promotes platelet disaggregation [16], such an impairment would put the vessel at risk for ischemic events due to thrombosis or vasospasm.

The present study suggests that if an ischemic event were to occur after cardiopulmonary bypass, tissue hypoxia would increase production of EDCF, thereby inducing or exacerbating coronary vasospasm. Indeed, such a sequence of events could lead to cardiovascular collapse at a time when the heart is exquisitely sensitive to ischemia because of preexisting myocardial disease or intraoperative injury.

The identity of the EDCF released in response to hypoxia has been elusive. The factor can diffuse [5], but has not been quantified in bioassay [17]. Previous studies have excluded catecholamines, serotonin, histamine, adenine nucleotides, and cyclooxygenase products as the contracting factor(s) induced by hypoxia [5, 13, 18]. In addition, the rapid onset and reversal of the contraction, coupled with the fact that hypoxic contraction can be

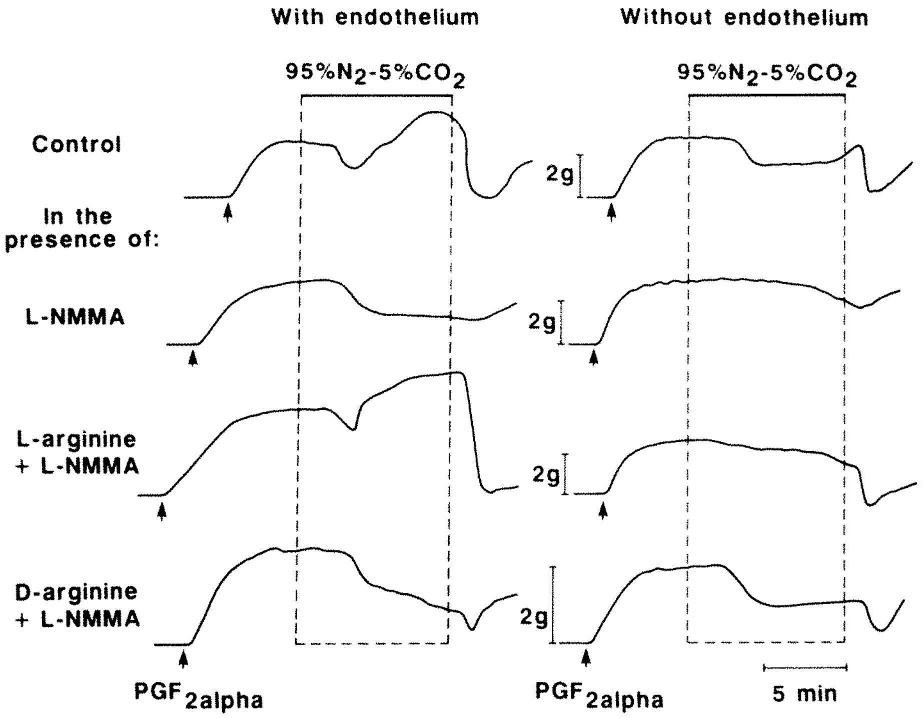


Fig 4. Isometric tension recordings of the effect of N^G*-monomethyl-*L*-arginine* (L-NMMA) *on endothelium-dependent hypoxic contraction in reperfused canine coronary segments. L-NMMA (10^{-5} mol/L) was added to the organ bath 10 minutes before contraction with prostaglandin $F_{2\alpha}$ ($PGF_{2\ alpha}$). When* L*-arginine (10^{-4} mol/L) and* D*-arginine (10^{-4} mol/L) were used, they were added to the organ bath 10 minutes before the addition of L-NMMA.*

blocked by calcium-channel blockers, make the vasoconstrictive peptide endothelin an unlikely candidate [19].

The present study demonstrates that endothelium-dependent hypoxic contraction can be inhibited by L-NMMA, a blocker of nitric oxide synthesis [20]. Nitric oxide has been identified as the active component of EDRF [21, 22], which is produced from L-arginine metabolism [23]. Martin [24] postulated that endothelium-dependent contractions to hypoxia might be due to a "down-regulation" of basally released EDRF. A basal level of EDRF is constantly being produced by many blood vessels [25]; impairment in EDRF production would remove the tonic relaxant effect on the vascular smooth muscle and, in effect, cause contraction. This hypothesis is supported by studies that demonstrate that hypoxia impairs the *stimulated* release of EDRF [11, 26]. With hypoxia, however, such a mechanism is implausible because inhibitors of EDRF do not modify endothelium-dependent contractions [5].

Although nitric oxide relaxes vascular smooth muscle, it also can combine with superoxide anion (O_2^-) to form the peroxynitrite anion ($ONOO^-$) [27]. $ONOO^-$ is very toxic and unstable, and it can decompose into highly reactive agents [28]. We hypothesize that O_2^- produced in the hypoxic milieu of the endothelial cell [29] combines with nitric oxide to form $ONOO^-$. $ONOO^-$ is then metabolized to EDCF or induces its synthesis (Fig 6). This hypothesis is supported by the finding that hypoxic contractions are augmented in arteries after reperfusion injury; such tissue is rich in oxygen-derived free radicals [30]. As free radicals also scavenge EDRF [31, 32] and inhibit endothelium-dependent vasodilation [33], free radical production by

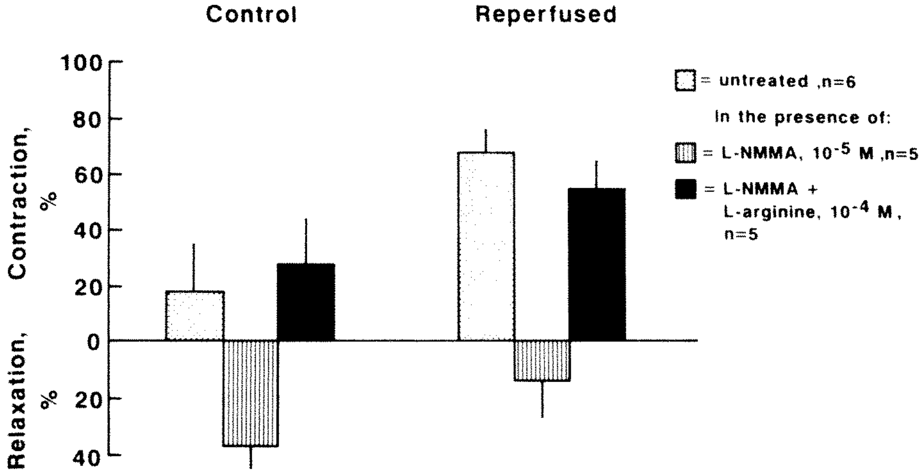
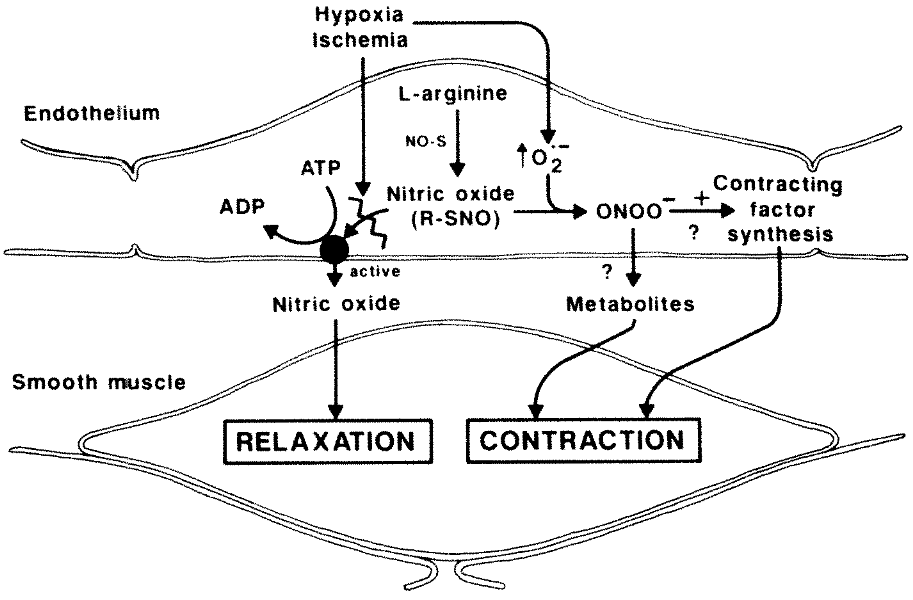


Fig 5. Effect of hypoxia on tension in contracted control and reperfused arteries with endothelium. Data are shown as mean ± standard error of the mean and expressed as percent of the initial contraction to prostaglandin $F_{2\alpha}$. (L-NMMA = N^G*-monomethyl-*L*-arginine.)*

Fig 6. Authors' hypothesis of the mechanism of endothelium-dependent hypoxic contraction. L*-arginine is utilized for endothelial cell production of nitric oxide (NO). During hypoxia, superoxide anion (O_2^-) formed in the hypoxic milieu of the endothelial cell combines with NO to form the peroxynitrite anion (ONOO$^-$). ONOO$^-$ is then metabolized to endothelium-derived contracting factor or induces its synthesis. The production of endothelium-derived contracting factor is enhanced after reperfusion injury secondary to an abundance of free radicals that can be utilized for ONOO$^-$ production. (ADP = adenosine diphosphate; ATP = adenosine triphosphate.)*



the reperfused endothelium would greatly increase vascular tone.

Coronary vasospasm appears to be an important but unrecognized cause of cardiovascular collapse after cardiac operations. Indeed, after global cardiac ischemia and reperfusion, coronary arteries with endothelium lose the ability to break the direct vasoconstrictive effect of aggregating platelets on the vascular smooth muscle [2]. Intracoronary platelet deposition that occurs after cardiopulmonary bypass [34] would favor increased vascular tone in the coronary circulation and might lead to myocardial ischemia. As the present study demonstrates, local tissue hypoxia caused by myocardial ischemia could augment production of EDCF and favor maintenance or exacerbation of coronary vasospasm.

It is also possible that systemic hypoxemia could induce vasoconstriction in the reperfused coronary circulation after cardiopulmonary bypass. Indeed, hypoxemia can occur after cardiac operations for a variety of reasons including hypoventilation, intrapulmonary shunting of blood, and during states of low cardiac output. The present study demonstrates that if hypoxemia were to occur, potentiated endothelium-dependent contraction of the reperfused coronary artery could decrease coronary blood flow and impair perfusion to the myocardium. Coupled with the direct depressed effect of hypoxemia on myocyte function, such a situation could rapidly lead to cardiovascular collapse.

References

1. Vanhoutte PM. The endothelium–modulator of vascular smooth-muscle tone. N Engl J Med 1988;319:512–3.
2. Pearson PJ, Lin PJ, Schaff HV. Global myocardial ischemia and reperfusion impairs endothelium-dependent relaxations to aggregating platelets in the canine coronary artery: a possible etiology of vasospasm following cardiopulmonary bypass. J Thorac Cardiovasc Surg (in press).
3. Hashimoto K, Pearson PJ, Schaff HV, Cartier R. Endothelial cell dysfunction after ischemic arrest and reperfusion: a possible mechanism of myocardial injury during reflow. J Thorac Cardiovasc Surg (in press).
4. Vanhoutte PM, Shimokawa H. Endothelium-derived relaxing factor and coronary vasospasm. Circulation 1989;80:1–9.
5. Rubanyi GM, Vanhoutte PM. Hypoxia releases a vasoconstrictor substance from the canine vascular endothelium. J Physiol 1985;364:45–56.
6. Iqbal A, Vanhoutte PM. Flunarizine inhibits endothelium-dependent hypoxic facilitation in canine coronary arteries through an action on vascular smooth muscle. Br J Pharmacol 1988;95:789–94.
7. Lin PJ, Pearson PJ, Schaff HV. Endothelium-dependent contractions to hypoxia in the human internal mammary artery. Surg Forum 1990;41:311–2.
8. Pearson PJ, Schaff HV, Vanhoutte PM. Acute impairment of endothelium-dependent relaxations to aggregating platelets following reperfusion injury in canine coronary arteries. Circ Res 1990;67:385–93.
9. Pearson PJ, Schaff HV, Vanhoutte PM. Long-term impairment of endothelium-dependent relaxations to aggregating platelets after reperfusion injury in canine coronary arteries. Circulation 1990;81:1921–7.
10. DeMey JG, Vanhoutte PM. Role of the intima in cholinergic and purinergic relaxation of isolated femoral arteries. J Physiol 1981;316:347–55.
11. DeMey JG, Vanhoutte PM. Heterogeneous behavior of the canine arterial and venous wall: importance of the endothelium. Circ Res 1982;51:437–9.
12. Furchgott RF, Zawadski JV. The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 1980;288:373–6.
13. DeMey JG, Vanhoutte PM. Anoxia and endothelium-dependent reactivity of the canine femoral artery. J Physiol 1983;335:65–74.
14. Radomski MW, Palmer RMJ, Moncada S. The role of nitric oxide and cyclic GMP in platelet adhesion to vascular endothelium. Biochem Biophys Res Commun 1987;148:1482–9.
15. Furlong B, Henderson AH, Lewis MJ, Smith JA. Endothelium-

derived relaxing factor inhibits in vitro platelet aggregation. Br J Pharmacol 1987;90:687–92.

16. Radomski MW, Palmer RMJ, Moncada S. Comparative pharmacology of endothelium-derived relaxing factor, nitric oxide and prostacyclin in platelets. Br J Pharmacol 1987;92:181–7.
17. Vanhoutte PM, Auch-Schwelk W, Boulanger C, et al. Does endothelin-1 mediate endothelium-dependent contractions during anoxia? J Cardiovasc Pharmacol 1989;13(Suppl 5): S124–8.
18. Katusic ZS, Vanhoutte PM. Anoxic contractions in isolated canine cerebral arteries: contribution of endothelium-derived factors, metabolites of arachidonic acid, and calcium entry. J Cardiovasc Pharmacol 1986;8(Suppl 8):S97–101.
19. Vanhoutte PM, Auch-Schwelk W, Boulanger C, et al. Does endothelin-1 mediate endothelium-dependent contractions during anoxia? J Cardiovasc Pharm 1989;13(Suppl 5):S124–8.
20. Rees DD, Palmer RMJ, Hodson HF, Moncada S. A specific inhibitor of nitric oxide formation from L-arginine attenuates endothelium-dependent relaxation. Br J Pharmacol 1989;96: 418–24.
21. Palmer RMJ, Ferrige AG, Moncada S. Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor. Nature 1987;327:524–6.
22. Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide. Proc Natl Acad Sci USA 1987;84:9265–9.
23. Palmer RMJ, Rees DD, Ashton DS, Moncada S. L-arginine is the physiological precursor for the formation of nitric oxide in endothelium-dependent relaxation. Biochem Biophys Res Commun 1988;153:1251–6.
24. Martin W. Basal release of endothelium-derived relaxing factor. In: Vanhoutte PM, ed. Relaxing and contracting factors. Clifton, NJ: Humana Press, 1988:171–2.
25. Rees DD, Palmer RMJ, Moncada S. Role of endothelium-derived nitric oxide in the regulation of blood pressure. Proc Natl Acad Sci USA 1989;86:3375–8.
26. DeMey J, Vanhoutte PM. Interactions between Na^+, K^+ exchanges and the direct inhibitory effect of acetylcholine on canine femoral arteries. Circ Res 1980;46:826–36.
27. Blough NV, Zafiriou OC. Reaction of superoxide with nitric oxide to form peroxynitrite in alkaline aqueous solution. Inorgan Chem 1985;24:3502–4.
28. Beckman JS, Beckman TW, Chen J, Marshall PA, Freeman BA. Apparent hydroxyl radical production by peroxynitrite: implications for endothelial injury from nitric oxide and superoxide. Proc Natl Acad Sci USA 1990;87:1620–4.
29. Ratych RE, Chuknyiska RS, Bulkley GB. The primary localization of free radical generation after anoxia/reoxygenation in isolated endothelial cells. Surgery 1987;102:122–31.
30. Zweier JL, Kuppusamy P, Lutty GA. Measurement of endothelial cell free radical generation: evidence for a central mechanism of free radical injury in postischemic tissue. Proc Natl Acad Sci USA 1988;85:4046–50.
31. Gryglewski RJ, Palmer RMJ, Moncada S. Superoxide anions play a role in the breakdown of endothelium-derived relaxing factor. Nature 1986;320:454–6.
32. Rubanyi GM, Vanhoutte PM. Superoxide anions and hyperoxia inactivate endothelium-derived relaxing factor. Am J Physiol 1986;250(Heart Circ Physiol 19):H822–7.
33. Stewart DJ, Pohl U, Bassenge E. Free radicals inhibit endothelium-dependent dilation in the coronary resistance bed. Am J Physiol 1988;255(Heart Circ Physiol 24):H765–9.
34. Feinberg H, Rosenbaum DS, Levitsky S, Silverman NA, Kohler J, LeBreton G. Platelet deposition after surgically induced myocardial ischemia. J Thorac Cardiovasc Surg 1982;84:815–22.

Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 16, 1992. The closing date for registration is August 1, 1991.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Pulmonary Sequelae of Prolonged Total Venoarterial Bypass: Evaluation With a New Experimental Model

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Total normothermic venoarterial bypass was established in 6 healthy pigs over a period of 18 hours. A heparin-coated closed extracorporeal system was used and no heparin was administered systemically. During the bypass period the main pulmonary artery was occluded and the heart was maintained in a beating state. All the animals maintained stable hemodynamics and normal blood gases during the entire period of bypass. In the postbypass period, the central hemodynamics continued to be stable while the arterial oxygen tension (inspired oxygen fraction = 0.21) decreased significantly ($p \leq 0.05$). The total body oxygen uptake, on the other hand, remained unaltered. All the animals died within 4 hours after weaning off the venoarterial bypass circuit on account of pulmonary edema in 2 and cardiac arrest in 4. Death was preceded by progressive pulmonary hypertension and lactacidosis in all the animals. Histological examination of the lungs showed pulmonary parenchymal damage ranging from interstitial edema to intraalveolar hemorrhage and parenchymal necrosis involving more than 80% of the pulmonary parenchyma. A normothermic total venoarterial bypass of 18 hours duration or more produces pulmonary edema of varying severity, pulmonary hypertension, pulmonary parenchymal necrosis, and lactacidosis in healthy juvenile pigs, resulting uniformly in their death. Despite these sequelae the systemic arterial hypoxemia may only be mild to moderate.

(Ann Thorac Surg 1991;51:794–9)

Total venoarterial bypass is routinely employed in open heart operations. This form of bypass is often prolonged as a first-line measure for postcardiotomy cardiac support [1–4]. Prolonged venoarterial bypass (extracorporeal membrane oxygenation) has also been employed for respiratory support in children and adults with varied levels of success [5, 6]. At present, extracorporeal membrane oxygenation is one of the few methods available for temporary support of patients with both pulmonary and cardiac failure [7].

During venoarterial bypass (VAB) the right cardiac output is reduced, and this reduction is directly proportional to the venous drainage of the right heart. In certain situations, the cardiac output from the right heart may be negligible. In this article we have studied the sequelae of 18 hours of total VAB at normothermia in an experimental model in which right cardiac output has been totally eliminated.

Material and Methods

Six Swedish native-breed male pigs with a mean body weight of 57 kg (range, 56 to 57 kg) were selected for this study. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

The animals were put to sleep by intramuscular injection of ketamine hydrochloride, 25 mg/kg body weight (Ketalar; Parke-Davis/Warner-Lambert, Morris Plains, NJ). Pentothal sodium (Pentothal Natrium; Abbot Laboratories, North Chicago, IL), 250 to 500 mg, was given intravenously before a tracheostomy was done. A No. 7 endotracheal tube was placed in the trachea and connected to a Siemens Elema Servo Ventilator 900 (Siemens-Elema AB, Stockholm, Sweden). Volume-controlled ventilation with an inspired oxygen fraction of 0.21 and a minute ventilation of 170 mL/kg body weight was instituted. End-tidal carbon dioxide concentration was continuously monitored by a capnograph (DATEX, Normocap pCO_2 & pO_2 monitor, Helsinki, Finland). Anesthesia and relaxation were maintained by continuous intravenous infusion of a mixture of Ketalar (300 mg/h) and pancuronium bromide (Pavulon; Organon Teknika, Boxtel, Holland; 20 mg/h). Central venous and arterial pressure lines were established through the neck vessels. An indwelling Foley catheter was placed in the urinary bladder through a suprapubic cystotomy. Prophylactic antibiotics (penicillin-streptomycin) were given every 12 hours. Four liters of intravenous fluids were given every 24 hours (glucose 10%, 2 L; albumin 5%, 1 L; Ringer's acetate, 1 L). Addi-

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tional intravenous fluids (isotonic 2.5% glucose/Rehydrex; KabiVitrum AB, Stockholm, Sweden) were administered to compensate for the urinary losses.

The experiments were conducted under regular monitoring of electrocardiogram, central arterial and venous pressure, urinary output, blood gas analysis, and body temperature. Blood samples were taken before and at the end of the experiment for routine hematology, blood biochemistry, and measurement of renal and liver function. Blood samples were also taken for analysis of pyruvates and lactates and immediately frozen in liquid nitrogen (in animals 4, 5, and 6). Only those animals with normal preexperiment central and peripheral hemodynamics and blood gases (inspired oxygen fraction = 0.21) were admitted into the study.

The chest was entered through a midline sternotomy and the heart was exposed. A pressure line was placed in the left atrium for pressure monitoring and blood sampling. A Swan-Ganz catheter was placed in the pulmonary artery for measurement of pulmonary artery pressure and cardiac output and for mixed venous blood sampling. Total body oxygen uptake was calculated from blood gas analysis of arterial and mixed venous blood, cardiac output, and the hemoglobin concentration at that particular interval using a computer program based on Kelman and Nun normograms for correction of blood oxygen tension, carbon dioxide tension, pH, and base excess for time and temperature [8]. Lung compliance (open chest and pleura) was obtained from the ventilator and was defined as V_T/P_{pause}, where V_T = tidal volume and P_{pause} = airway pressure at the end of inspiratory pause. Functional residual capacity was determined both before and at the end of the experiment by a computerized tracer gas wash-out technique [9].

Venous return to the heart-lung machine was provided by placing two 28F wire-reinforced cannulas (Research Medical Inc, Salt Lake City, UT) in the inferior vena cava and in the right ventricle (across the tricuspid valve). Oxygenated blood from the heart-lung machine was returned to the animal through a 20F wire-reinforced cannula in the right femoral artery. The heart-lung machine comprised a hollow-fiber membrane oxygenator (Maxima; Medtronic, Anaheim, CA) with its built-in heat exchanger, a nonocclusive roller pump, and a hypothermia machine (Gambro, Lund, Sweden). The venous return to the heart-lung machine was regulated by a servo-controlled collapsible balloon (Carmeda AB, Stockholm, Sweden) interposed in the venous line. The extracorporeal bypass circuit was a closed one and had previously been treated by a Carmeda Bio-active Surface (Carmeda AB) [10, 11].

No heparin was administered to the animals during the entire experiment. The extracorporeal circuit was primed with 5% albumin (970 mL) and the temperature of the perfusate was regulated to maintain the rectal temperature of the animals between 37.0° and 38.5°C. After the initiation of bypass, maximum possible blood flow was diverted through the extracorporeal circuit and a blood/oxygen gas ratio of 1:1 was held in the membrane oxygenator. A tape was passed around the main pulmonary artery twice and was tightened over a snare to occlude the flow of blood from the right ventricle into the main pulmonary artery. The ventilator was now reset to the dead-space ventilation (volume-controlled ventilation = 1 L/min; frequency = 20/min, positive end-expiratory pressure = 5 cm H_2O, and inspired oxygen fraction = 0.21). Ventilating gases were supplemented with CO_2 to maintain end-tidal CO_2 concentration within normal limits.

After 18 hours of total VAB, the band and the snare around the main pulmonary artery were removed and the animals were weaned off the bypass over a period of 1 hour. Bypass flows were reduced by 1 L every 10 minutes in a standardized manner, and during this period a thorough bronchial toilet, suctioning, and intermittent manual lung inflation were performed. During the period of weaning and after it, the ventilation was reset to values similar to those at the start of the experiment. At the conclusion of the experiment, autopsy of the heart and lungs was performed in all the animals. Two pieces of pulmonary tissue were randomly excised from the right and the left lung from both ventral and dorsal lung segments for histopathology. Pulmonary artery branches were meticulously dissected and examined for any macroscopic thromboemboli. Histopathological examination of the lung samples was carried out under a light microscope after staining with hematoxylin and eosin.

The results were evaluated statistically using the Wilcoxon signed ranks test.

Results

During 18 hours of pulmonary artery occlusion, VAB provided a stable hemodynamics in all the animals. Systemic and mixed venous blood gases remained within the normal limits in all animals. Routine renal and liver function studies performed before and at the end of the experiment were also within normal limits. With the onset of bypass and for the entire period after it, all animals showed a decrease in both the hemoglobin and the hematocrit values by about 25% each on account of hemodilution. Bleeding from the open chest wound was minimal, and no external blood transfusion was given. All animals maintained normal diuresis, and the urine remained clear.

All the animals died within 4 hours (range, 0.5 to 4 hours) of cessation of VAB. Death was preceded by massive pulmonary edema in 2 (animals 3 and 5) and cardiac arrest in the remaining 4 animals. All the animals showed a significant ($p \leq 0.05$) deterioration in the arterial and mixed venous blood oxygen tension (inspired oxygen fraction = 0.21) in the immediate postbypass period. The arterial oxygen tension values, however, improved spontaneously and successively in all animals. The total body oxygen uptake in the postbypass period (before death) showed an increase in 3 animals (animals 1, 2, and 4) with a slight decrease in the other 2 animals (animals 3 and 5) when compared with the prebypass values (Table 1). Arterial and mixed venous blood carbon dioxide tension also showed a significant increase ($p \leq 0.05$) in the

Table 1. Hemodynamics and Respiratory Mechanics[a]

Variable	Prebypass	Postbypass[b]
PVR (dynes · s^{-1} · cm^{-5})	153 ± 35	489 ± 157
SVR (dynes · s^{-1} · cm^{-5})	1,050 ± 89	1,144 ± 35
CO (L/min)	5.9 ± 0.3	4.2 ± 0.9
O_2 uptake (mL/min)	169 ± 28	228 ± 34
C_L (mL/cm H_2O)	32 ± 2.3	20 ± 2.2[c]
FRC[d] (mL)	1,375 ± 86	991 ± 112

[a] Values are shown as mean ± standard error of the mean. [b] Last regular value before death. [c] $p \leq 0.05$ versus prebypass. [d] n = 4.

C_L = pulmonary compliance; CO = cardiac output; FRC = functional residual capacity; O_2 uptake = total body O_2 uptake; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

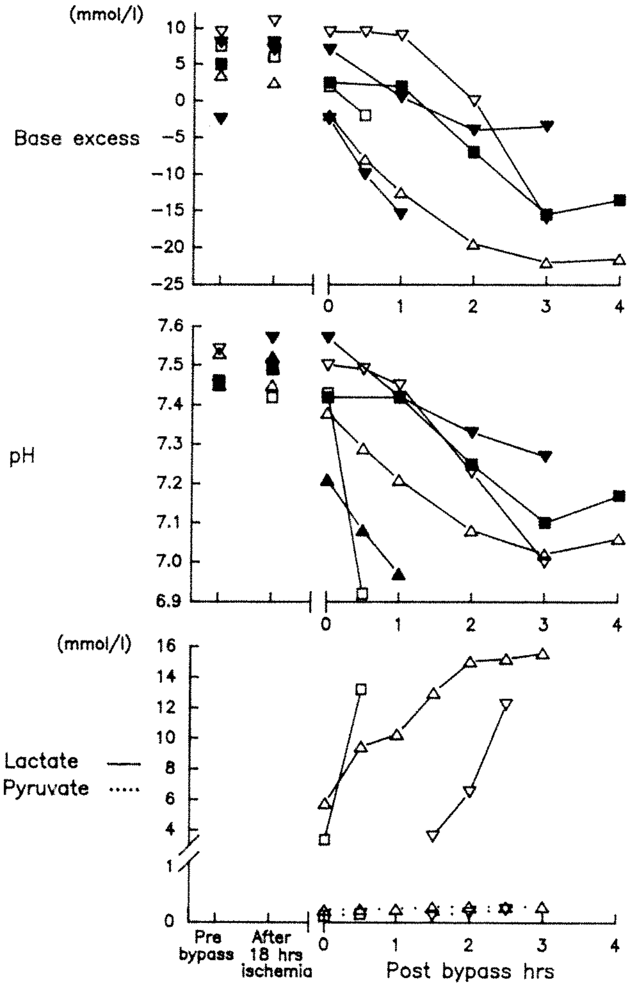

Fig 1. Development and progression of metabolic acidosis after 18 hours of venoarterial bypass with occluded main pulmonary artery. Blood lactate levels (solid lines; *normal values: 0.09 to 0.19 mmol/L) showed successive increase while pyruvates* (dotted lines; *normal values: 0.46 to 0.77 mmol/L) remained unaltered. (▼, ■, ▲, ▽, □, △ = animals 1, 2, 3, 4, 5, and 6, respectively.)*

immediate postbypass period (Table 2), and this increase was most marked in animals 3 and 5. In the remaining animals, these values showed only a marginal increase.

The striking biochemical alteration in the postbypass period and preceding death was a progressively increasing severe acidosis in all the animals, with the lowest registered pH values in the range of 6.92 and 7.27 (mean, 7.06) and the base excess in the range of −3.5 and −21.5 mmol/L (mean, −15.0 mmol/L) (Fig 1). Animals 3 and 5 registered the lowest pH values (6.92 and 6.97), but their terminal negative base excess values were no different from those in animals 2, 4, and 6 (see Fig 1). Lactates in the arterial blood increased in direct proportion to the increase in the negative base excess (see Fig 1). Pyruvates, on the other hand, remained within normal limits. Pulmonary vascular resistance increased in all animals except 1 by an overall average of about 200%. The systemic vascular resistance, on the other hand, remained essentially unchanged (see Table 1). Lung compliance decreased significantly ($p \leq 0.05$), and functional residual capacity also showed a decrease (see Table 1).

At autopsy, the total lung weight varied between 630 and 1,550 g (mean, 986 g). The total lung weight in animals 3 and 5 was almost two times (mean, 1,375 g) greater than that of the others (mean, 726 g). The dorsal dependent segments of the lungs showed massive atelectasis in all the animals, and these were heavier compared with the ventral nondependent segments, which were airy and light. All the segments of the lungs were, however, inflatable on manual inflation by an Ambu bag (Laerdal, Stavanger, Norway). No macroscopic emboli

Table 2. Blood Gas Analysis[a]

Variable	Prebypass	After 18 Hours of Bypass	Postbypass Hours					
			0	0.5	1	2	3	4[b]
PO_2								
Arterial	113 ± 19	190 ± 40	168 ± 68	52 ± 7[c]	52 ± 5[c]	55 ± 8	61 ± 5	64
Mixed venous	37 ± 2	. . .	37 ± 6	21 ± 1[c]	23 ± 3	28 ± 4	21 ± 2	26
PCO_2								
Arterial	39 ± 3	41 ± 2	45 ± 6	60 ± 11[c]	51 ± 10[c]	46 ± 6	50 ± 5	32
Mixed venous	46 ± 4	. . .	52 ± 8	76 ± 17[c]	74 ± 16	62 ± 3	72 ± 12	48

[a] Values are shown as mean ± standard error of the mean in millimeters of mercury. [b] n = 3. [c] $p \leq 0.05$ versus prebypass.

PCO_2 = carbon dioxide tension; PO_2 = oxygen tension.

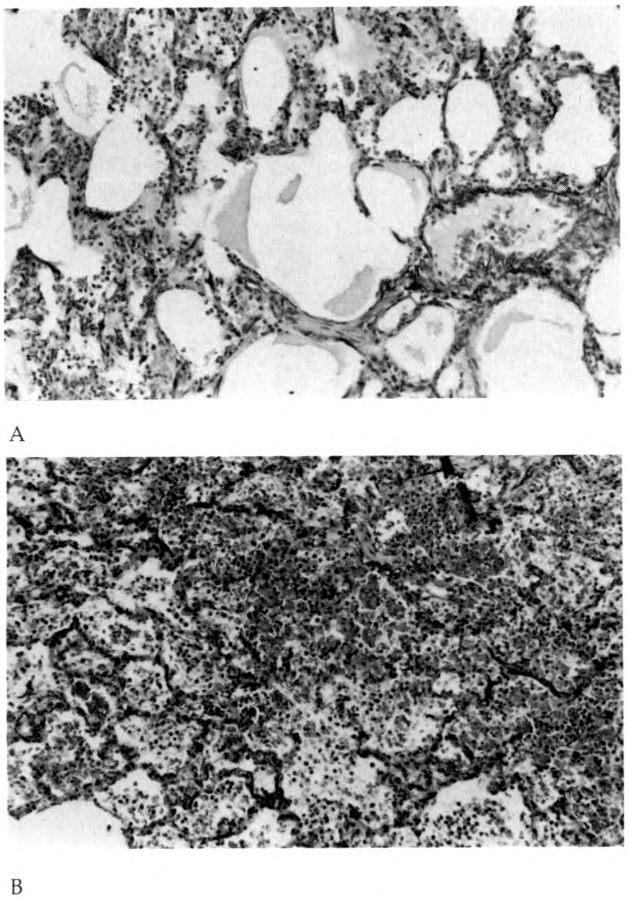

Fig 2. (A) Diffuse alveolar damage with prominent hyaline membranes. (Hematoxylin and eosin, Verhoff-Van Gieson ×50 enlarged ×3.7 = ×185 before 32% reduction.) (B) Massive intraalveolar hemorrhage, acute inflammation, and necrosis. (Hematoxylin and eosin, Verhoff-Van Gieson ×50 enlarged ×3.7 = ×185 before 32% reduction.)

were seen in the large pulmonary artery branches. Heart was slightly edematous in all the animals and showed macroscopic focal endocardial and subendocardial hemorrhages, more marked in the left ventricle.

The microscopic changes in the pulmonary parenchyma corresponded to an exudative stage of diffuse alveolar damage. Protein-rich and low-protein interstitial and intraalveolar edema was accompanied by massive alveolar capillary congestion. A distinct hyaline membrane was seen in many areas (Fig 2A). Intraalveolar hemorrhage, fibrin exudation, and inflammation involved more than 80% of the pulmonary tissue examined (Fig 2B). Multiple thrombi were seen in the small alveolar capillaries. Early necrotic changes were seen in the worst affected areas. The subpleural regions were relatively well preserved despite patchy distribution of the pulmonary lesions.

Comment

Salient features of the experimental model employed in this study are (1) total normothermic pulmonary artery occlusion of 18 hours' duration with intact bronchial and lymphatic circulation of the entire lung, (2) beating heart in the presence of an occluded main pulmonary artery to ensure good cardiac function in the postbypass period, (3) undisturbed drainage and ejection of the bronchial venous blood from the left heart during the bypass period, (4) no manipulation of the lungs before or during the experiment, (5) provision of a normal or near-normal alveolar gas composition by carbon dioxide supplementation of the ventilating gases, and (6) heparin-free bypass with minimal operative and postoperative blood loss. Efficacy of the Carmeda Bioactive Surface during a 24-hour period of heparin-free bypass in healthy pigs has been reported earlier by us [12].

Most of the experimental work done to study the ischemic tolerance of the lungs has been focused on a model pertinent to the donor for clinical lung transplantation. These donor lung models lack both pulmonary and bronchial arterial supply and the lymphatic drainage. Studies with these isolated lung models have shown that the lung tolerates warm ischemia up to 4 hours [13, 14] and hypothermic ischemia up to 5 hours relatively well [15, 16]. The ischemic intolerance has been shown to manifest itself in the form of pulmonary edema and attendant hypoxia-reperfusion injury [17, 18].

In situ experimental studies with unilateral normothermic pulmonary artery ischemia have shown an unexplained secondary effect on the contralateral perfused and ventilated lung in the reperfusion period [19]. Further, pulmonary hilar stripping and the attendant physical manipulation of the lung have also been shown to affect lung function significantly [20, 21]. The present experimental model does not have these shortcomings. An 18-hour period of total VAB was selected for this study because pulmonary artery ischemic periods up to 12 hours have been shown not to result in reperfusion-induced pulmonary edema [22]. Our initial pilot experiments with fibrillating hearts (leaving the pulmonary artery unoccluded) showed varying grades of antegrade blood flow across the pulmonary vascular bed and impaired cardiac function in the postbypass period. These observations motivated us to embark on the present model.

In the present study, all the animals maintained stable hemodynamics and had normal blood gases through the entire 18-hour period of total VAB. In the postbypass period all the animals showed tachycardia and an increased arteriovenous oxygen difference, suggesting a hypokinetic peripheral circulation. Further, the pulmonary vascular resistance increased by about 200%, and this might have contributed to the postbypass decrease (about 30%) in cardiac output (see Table 1).

Total VAB of 18 hours' duration resulted in a significant decrease in arterial and venous oxygen tension in the early postbypass period. However, the postbypass total body oxygen uptake showed only a slight variation from that of the prebypass period (see Table 1). In fact, only animals 3 and 5 registered a slight decrease in postbypass total body oxygen uptake, and both these animals died in the early postbypass period (60 and 30 minutes, respectively) of severe pulmonary edema. These 2 animals registered the maximal increase in pulmonary vascular resistance (350% and 430%, respectively) and showed a blood gas picture (see Fig 1) of combined metabolic and respiratory acidosis (arterial oxygen tension = 55 and 68 mm Hg, respectively, and arterial carbon dioxide tension = 90 and 81 mm Hg, respectively). The serial blood gas analysis in the remaining 4 animals was dominated almost entirely by metabolic acidosis. Animal 6 had near-normal arterial oxygen and carbon dioxide tension values through the entire postbypass period and died 4 hours after the cessation of VAB on account of increasing negative base excess (−21.5) and decreasing pH (−7.06). In the presence of relatively normal systemic hemodynamics and a relatively unaltered total body oxygen uptake, the development of severe and rapidly progressive metabolic acidosis in the postbypass period cannot therefore be entirely explained on the basis of mild systemic hypoxia. That the acidosis manifested itself first after the cessation of VAB is suggestive of ischemic damage of the pulmonary parenchyma and a reperfusion phenomenon wherein the lactates from the ischemic lungs are washed out into the systemic circulation. Lactates in the blood increased in direct relationship to the increasing negative base excess in the postbypass period (see Fig 1). Modry and Chiu [23] have shown that a 24-hour interruption of pulmonary arterial blood flow in the canine lung produces a significant decrease in the ratio of adenosine triphosphate to adenosine diphosphate, a decrease in glycogen levels, and an increase in tissue lactate levels.

Light microscopy of the lungs showed morphological changes varying from frank pulmonary edema to intraalveolar hemorrhage and pulmonary parenchymal necrosis in different stages of development in the same specimen. More than 80% of the pulmonary parenchyma was involved with these changes. These histopathological changes can explain the significant decrease in pulmonary compliance and the decrease in functional residual capacity. A twofold increase in pulmonary vascular resistance may partly be ascribed to the massive pulmonary parenchymal damage with thrombotic obstruction of the pulmonary capillary bed. All the animals died within 4 hours of reperfusion, and this period may be too short to allow complete expression of the morphological changes induced on account of pulmonary artery ischemia. The form and the extent of these pathological pulmonary changes together with rapidly progressive metabolic acidosis culminating in the death of all animals would suggest that the pulmonary parenchymal changes induced are irreversible.

In the light of these observations, the deterioration in arterial blood gases was, however, not of such magnitude as to explain early death of all the animals. In this context it may be recalled that these animals were ventilated throughout with an inspired oxygen fraction of only 0.21. Moreover, during the 18-hour period of total VAB the lungs were minimally ventilated (dead space ventilation), and development of persistent atelectases under these circumstances is unavoidable. Hypoxia, on the other hand, has been reported to be the principal alteration in resected warm ischemic lungs preserved for periods beyond 4 hours [18]. It is possible that the bronchial blood supply alone is sufficient to maintain the integrity of the alveolar gas exchange apparatus over long periods of pulmonary artery ischemia. In this connection it may be pointed out that the anatomy of the bronchial circulation in pigs resembles closely that of humans [24].

Functional and histopathological changes occurring in lungs as a sequel to conventional cardiopulmonary bypass have been ascribed to complement activation [25]. We, however, doubt that the pulmonary changes encountered in this study were, entirely or to a major extent, due to complement activation because a 24-hour period of near-total venovenous bypass in pigs (employing the Carmeda heparin-coated system) was followed by normal pulmonary gas exchange and normal pulmonary hemodynamics [12]. In this regard it may be pointed out that the heparin-coated system used in this study has been shown to be more biocompatible than one without the heparin coating [26].

To conclude, an 18-hour period of total VAB at normothermia in healthy juvenile pigs is followed by pulmonary edema of varying intensity, pulmonary hypertension, severe metabolic acidosis, and global microscopic pulmonary parenchymal damage, which is attended with 100% mortality. Despite these sequelae the systemic arterial hypoxemia may only be mild to moderate. The minimal right cardiac output required for optimal lung preservation during VAB at normothermia remains to be seen. Experiments in this regard are underway in our laboratory.

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References

1. Pennington DG, Merjavy JP, Codd JE, et al. Extracorporeal membrane oxygenation for patients with cardiogenic shock. Circulation 1984;70(Suppl 1):130–7.
2. Birnbaum PL, Henderson MJ, Weisel RD, et al. Extracorporeal circulatory assist devices. Trans Am Soc Artif Intern Organs 1987;33:190–3.
3. Nawa S, Yamada M, Teramoto S. Evaluation of conventional circulatory assist devices, intraaortic balloon pumping, venoarterial bypass and extracorporeal membrane oxygenation. Chest 1989;95:261–6.
4. Weinhaus L, Canter C, Noetzel M, McAlister W, Spray TL. Extracorporeal oxygenation for circulatory support after repair of congenital heart defects. Ann Thorac Surg 1989;48:206–12.
5. Ortiz RM, Cilley RE, Bartlett RH. Extracorporeal membrane oxygenation in pediatric respiratory failure. Pediatr Clin North Am 1987;34:39–46.
6. Zapol WM, Snider MT, Hill JD, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. JAMA 1979;242:2193–6.
7. Redmond CR, Graves ED, Falterman KW, Ochsner JL, Arensman RM. Extracorporeal membrane oxygenation for respiratory and cardiac failure in infants and children. J Thorac Cardiovasc Surg 1987;93:199–204.

8. Kelman GR, Nunn JF. Normograms for correction of blood pO_2, PCO_2, pH and base excess for time and temperature. J Appl Physiol 1966;21:1484–90.
9. Larsson A, Linnarsson D, Jonmarker C, Jonson B, Werner O. Measurement of lung volume by sulfur hexafluoride washout during spontaneous and controlled ventilation. Anesthesiology 1987;67:543–50.
10. Larm O, Larsson R, Olsson P. A new non-thrombogenic surface prepared by selective covalent binding of heparin via a modified reducing terminal residue. Biomater Med Devices Artif Organs 1983;11:161–73.
11. Pasche B, Kodama K, Larm O, Olsson P, Swedenborg J. Thrombin inactivation on surfaces with the covalently bonded heparin. Thromb Res 1986;44:739–48.
12. Koul B, Wetterberg T, Sjöberg T, et al. Veno-right ventricular bypass as total extracorporeal lung assistance (ECLA)—an experimental study. J Thorac Cardiovasc Surg (in press).
13. Veith FJ, Koerner S, Torres M, Attai L, Gliedman ML. Functional evaluation of lungs transplanted after varying ischemic intervals and after preservation by mechanical ventricular assistance. Ann Thorac Surg 1969;7:446–58.
14. Ardekarni RG, Faber LP, Beattie EJ. Pulmonary function after various periods of ischemia in the canine lung. J Thorac Cardiovasc Surg 1970;59:607–12.
15. Joseph WL, Morton DL, Adkins PC. Influence of ischemia and hypothermia on the ability of the transplanted primate lung to provide immediate and total respiratory support. J Thorac Cardiovasc Surg 1971;62:752–62.
16. Connaughton PJ, Bahuth JJ, Lewis FJ. Lung ischemia up to six hours: influence of local cooling in situ on subsequent pulmonary function. Dis Chest 1962;41:404–8.
17. Stuart RS, Monte SMDL, Baumgartner WA, et al. Successful four hour hypothermic lung storage with Euro-Collins solution: a simplified model assessing preservation. J Heart Transplant 1984;3:346–50.
18. Wang L, Yoshikawa K, Miyoshi S, et al. The effect of ischemic time and temperature on lung preservation in a simple ex vivo rabbit model used for functional assessment. J Thorac Cardiovasc Surg 1989;98:333–42.
19. Bishop MJ, Chi EY, Cheney FW. Lung reperfusion in dogs causes bilateral lung injury. J Appl Physiol 1987;63:942–50.
20. Garzon AA, Cheng C, Pangan J, Karlsson KE. Hypothermic hyperbaric lung preservation for twenty-four hours with replantation. J Thorac Cardiovasc Surg 1968;55:546–54.
21. Prop J, Ehrie MG, Crapo JD, Nieuwenhuis P, Wildevuur CRH. Reimplantation response in isolated graft lungs. J Thorac Cardiovasc Surg 1984;87:702–11.
22. Horgan MJ, Lum H, Malik AB. Pulmonary edema after pulmonary artery occlusion and reperfusion. Am Rev Respir Dis 1989;140:1421–8.
23. Modry DL, Chiu RC. Pulmonary reperfusion syndrome. Ann Thorac Surg 1979;27:206–15.
24. McLaughlin RF, Tyler WS, Canada RO. A study of subgross pulmonary anatomy in various mammals. Am J Anat 1961; 108:149–65.
25. Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–57.
26. Nilsson L, Storm KE, Thelin S, et al. Heparin-coated equipment reduces complement activation during cardiopulmonary bypass in the pig. Artif Organs 1990;14:46–8.

REVIEW OF RECENT BOOKS

Surgery for Heart Valve Disease

Edited by Endre Bodnar
ICR Publishers, 1990
971 pp, illustrated, $140.00

Reviewed by Laurence H. Coffin, MD

Surgery for Heart Valve Disease represents the proceedings of a 1989 symposium held in London organized by Drs Endre Bodnar and Robert Frater. A broad spectrum of international contributors and attendees are represented. This 971-page volume comprises 89 papers, each with individual verbatim published discussion. Within these data, one will find discussions of such wide-ranging questions as the age factor in heart valve surgery, repair versus replacement of heart valves, selection of the appropriate device, timing of operation, reoperations, and operation for combined ischemic and valvar lesions. What one will not find, however, is detailed "how to do it" coverage of cardiac valvar operations. In particular, only a limited discussion of the principles of mitral valvar reconstruction popularized by Dr Alain Carpentier is included. Catheter balloon valvoplasty is dignified by inclusion in this surgical program.

My overall impression of the symposium is that it presents a myriad of individual valve operation statistics and small series, each making their individual points, interspersed with salty and amusing discussion. As such it would be useful for a practicing cardiac surgeon or cardiologist to scan this book, for an involved researcher to read the specific sections of interest to him or her in detail, or for a resident in cardothoracic surgery to be aware of the book as a potential source, but it would be of very limited value to a more junior house officer or medical student.

Unfortunately, like so many well-intentioned symposia, the gain in entropy obtained by exchange of ideas cools off long before the documentation of the meeting reaches a wider medical public. This volume will assume a position on the book shelf of most cardiac surgeons along with the proceedings of similar valve surgery symposia that preceded it since the fall of 1960.

Burlington, Vermont

Hospital Mortality and Long-Term Survival After Pulmonary Resection in the Elderly

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We have studied the hospital mortality and long-term survival in two groups of patients: those between 50 and 69 years of age (group 1, n = 136) and those older than 70 years of age (group 2, n = 43). The two groups were similar in terms of the distribution of histological type and postsurgical staging. The patients were treated by either lobectomy or pneumonectomy; the lobectomy rate was similar in both groups: 61% and 51% (not significant). Hospital mortality for group 1 was 4.4% and for group 2, 6.9%. Mortality was higher in both groups after pneumonectomy compared with lobectomy, but this was not significant (group 1, 6.2% versus 1.9%; group 2, 9.1% versus 4.7%). Hospital mortality after pulmonary resection was greater in the elderly, but this was not significant (lobectomy: 1.9% [group 1] versus 4.7% [group 2]; pneumonectomy: 6.2% [group 1] versus 9.1% [group 2]. The overall long-term survival at 2 and 4 years was 62.3% and 50.0% for group 1 and 72.5% and 66.6% for group 2. We suggest that the operative risk in the elderly is not prohibitive and the long-term results are acceptable. Patients should not be denied operation on the basis of age alone.

(Ann Thorac Surg 1991;51:800–3)

The incidence of lung cancer in the elderly is rising steeply among men and women. In men older than 75 years the incidence has overtaken that of the two other age cohorts (55 to 64 years and 65 to 74 years); indeed, the incidence in the youngest age group (55 to 64 years) has remained constant for many years (Fig 1) [1]. Although the incidence of lung cancer in women is lower, the trend remains the same.

It is a commonly held view that cancer, when it develops in the elderly, pursues a less aggressive course. This may be the case with some tumors, but there is no evidence that this is the case with carcinoma of the lung. The percentage survival of all patients with a diagnosis of carcinoma of the bronchus, regardless of the cell type or treatment received, is adversely affected by the age of that patient at the time of registration. The elderly group (75 to 84 years) fares worse than the two younger groups (Fig 2) [2].

Actuarial survival in the elderly seems to be increasing throughout the western world. At the age of 70 a man can expect on average to live another 10.4 years, and for women this rises to 13.9 years; at the age of 80 years this has fallen to 6.1 and 8.6 years, respectively [3]. Such a patient with carcinoma of the lung will almost certainly die prematurely.

As with all patients, the only hope of a cure is offered by operation, but at what risk? The risk of operation in those with concomitant respiratory or cardiac disease is well known. As more and more smokers are surviving into their seventies and being seen as candidates for pulmonary operation, is age also a factor to be taken into account? To answer this question we have studied the hospital mortality and long-term survival of those older than 70 years undergoing lung resection.

Material and Methods

Over the 4-year period, 1983 to 1986, a total of 370 patients with carcinoma of the bronchus older than 50 years were referred to a single surgeon. A strict protocol for the preoperative staging of all potential surgical candidates was followed (Fig 3). The suitability of the tumor for resection was evaluated by previously well-established criteria, which are shown in the algorithm (see Fig 3). At operation careful mediastinal node dissection was carried out, and these N2 lymph node groups as defined by Naruke and associates [6] were sent separately for histological analysis. If there was any evidence of macroscopic N2 disease, then an urgent frozen section was performed. The relevant N1 nodes were those contained within the resected specimen and were not routinely examined at operation.

Results

Of these 370 patients, only 179 (48.4%) were found to be suitable by these criteria for pulmonary resection. This surgical group was subdivided into two age groups, those between 50 and 69 years of age (group 1) and those older than 70 years (group 2). Group 1 consisted of 136 patients (76.0%) with a median age of 60.6 years; in group 2 there were 43 patients (24%) with a median age of 72.7 years.

All statistical analysis was by the χ^2 test with appropriate use of Yates' correction for small numbers [7].

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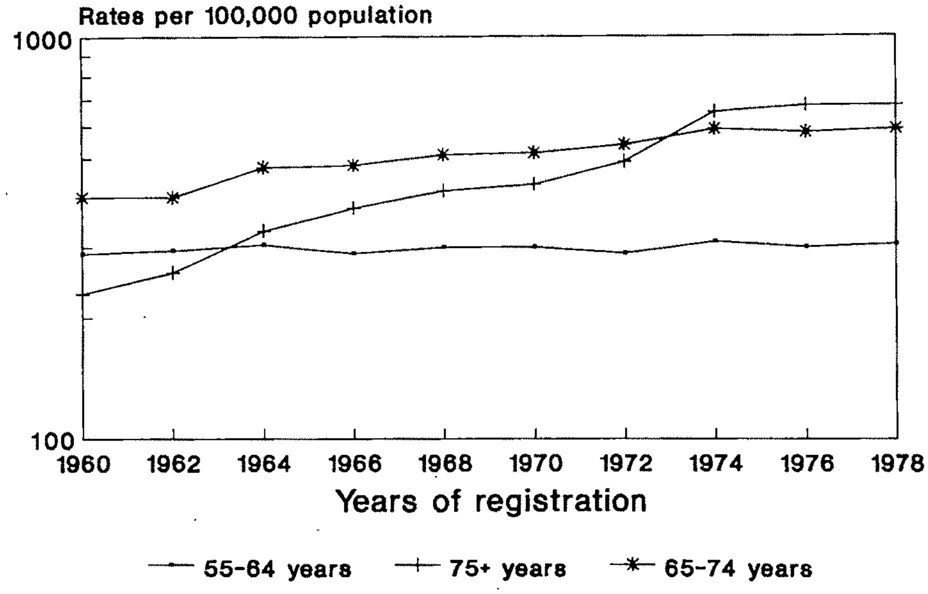


Fig 1. The incidence of lung cancer in men in England and Wales [1].

Pathological examination of the resected specimen gave a final histological diagnosis (Table 1) and a postoperative staging (Table 2). Although adenocarcinoma would appear to be more common in group 1 and large cell tumors in group 2, there is no statistical difference in the distribution of the four tumor types between the two groups. After postoperative staging (see Table 2), 50% of patients in both groups were classed as being in stage I; there was no significant difference in the postoperative staging of the two groups.

In group 1 61% of the patients underwent pneumonectomy, whereas in group 2 only 51% did so; this was not significant. Hospital mortality was defined as any death in the hospital after operation, regardless of the time elapsed. The overall hospital mortality was 5.0% (9/179). In group 1 there were six deaths out of 136 patients giving a hospital mortality of 4.4%; in group 2, 3 out of 43 patients died (6.9%; not significant by χ^2 test). When this mortality was examined with regard to the type of resection performed (lobectomy versus pneumonectomy), in both groups hospital mortality was greater in those patients undergoing pneumonectomy. The overall mortality after pneumonectomy was 6.7% compared with 2.7% after lobectomy. In group 1 6.0% (5/83) of patients died after pneumonectomy whereas there was only one death after lobectomy (1/53), a mortality of 1.9%. In group 2 the figures were 9.1% (2/22) and 4.7% (1/21) for pneumonectomy and lobectomy, respectively. This increased mortality after pneumonectomy was not significant in either group (χ^2). The apparent increased hospital mortality after pulmonary resection in elderly patients, 4.7% versus 1.9% for lobectomy and 9.1% versus 6.2% for pneumonectomy, was not significant (Table 3); the possibility of a type II error must, however, be borne in mind.

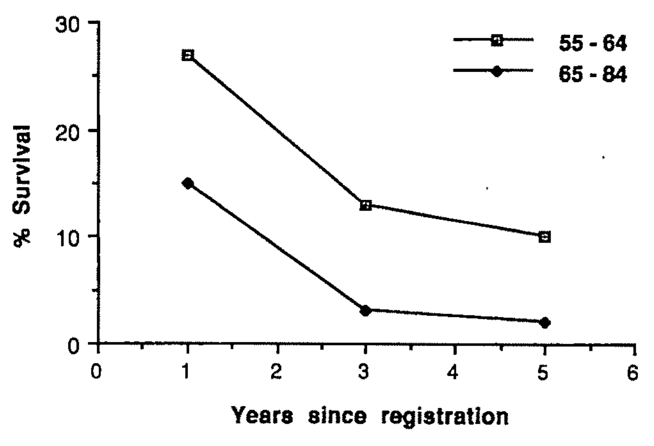


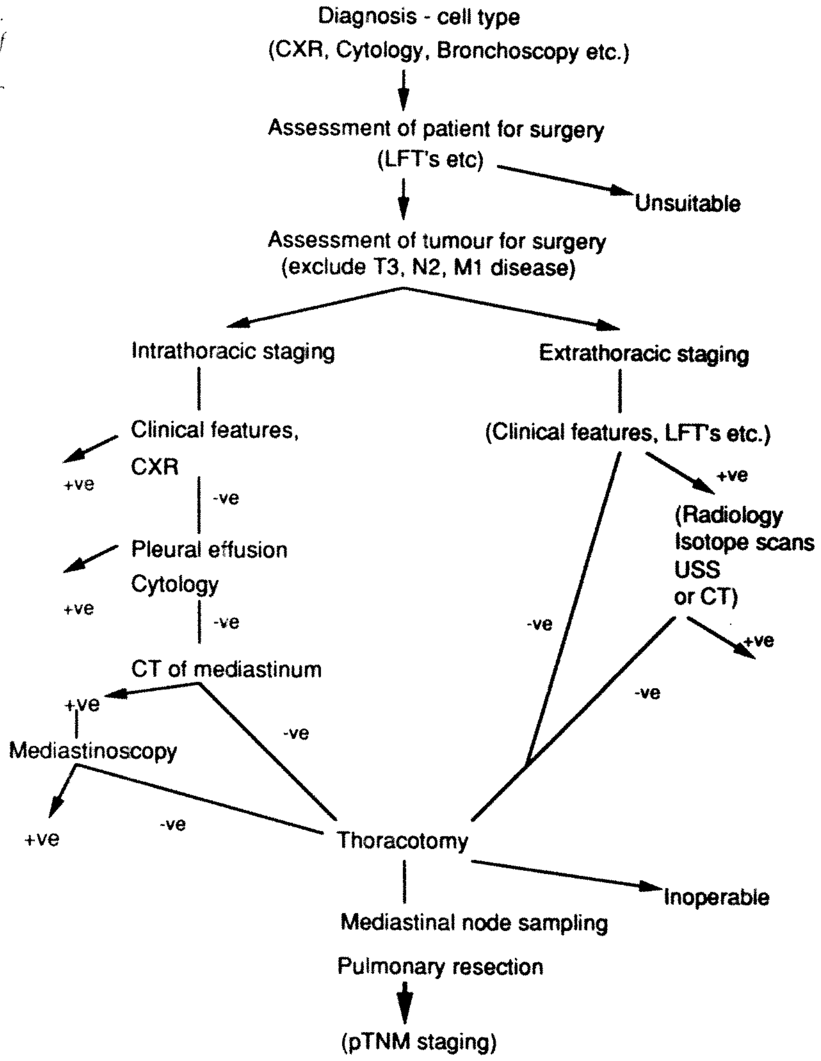
Fig 2. Relative survival rates of male patients with lung cancer registered in England and Wales in 1981 [2]. (□ 55–64 years old; ◆ 65–84 years old.)

The overall 2-year survival, excluding postoperative deaths, after pulmonary resection was 62.3% for group 1 and 72.5% for group 2, decreasing to 50% and 66.6% after 4 years. This overall survival was examined with regard to both pathological staging (Table 4) and histological type (Table 5). The size of the groups followed up for 4 years was much smaller, with only 61 in group 1 and 21 in group 2. The small numbers involved in the various subgroups mean that statistical analysis was not a realistic proposition.

Comment

All patients were subjected to the same preoperative evaluation in respect to patient fitness and tumor staging. There was no difference in the type of operation performed, and the distribution of histology and pathological staging between the two groups appeared to be the same; the two groups were well matched and seemed only to differ on the basis of age. However, patient selection must differ between the two groups; for example younger patients are fitter, tend to be more readily referred for operation, and may be subjected to more extensive oper-

Fig 3. Preoperative staging of non–small lung cancer. (Adapted from Spiro SG, Golastraw P. The staging of lung cancer. Thorax 1984;39:401–7.) (CT = computed tomography; CXR *= chest roentgenogram;* LFT *= liver function test;* pTNM *= postsurgical treatment-pathological staging;* USS *= ultrasonic scanning;* +ve *= positive;* −ve *= negative.)*



ation in an attempt to gain a long-term cure. This must be borne in mind when we compare these two groups and compare these results with the work of others.

Our findings with regard to hospital mortality are in keeping with many workers who have found an increased mortality after pneumonectomy compared with lobectomy. In 1983 the Lung Cancer Study Group of North America [8], in a retrospective analysis of 2,200 surgical resections for lung cancer, found a 6.2% mortality after pneumonectomy; this was significantly higher than that for lobectomy, which was 2.9%. The overall mortality rates in our study were very similar, 6.8% and 2.7%, respectively, and this did not attain significance probably due to the smaller numbers involved. It is to be noted that the overall pneumonectomy rate in this study of 51% was very different from that reported by the Lung Cancer Study Group of North America of only 18% and by the Sloan-Kettering Memorial Institute, whose rate was only 8.0% [9].

The majority of studies into the relationship of hospital mortality and patient age were in the 1970s and early 1980s: Bates [10] in 1970 reported hospital mortality of 23.0% after pneumonectomy and 13.0% after lobectomy; Kirsh and associates [11] in 1976 gave figures of 17.0% and 14.0%. In an analysis of 961 patients undergoing thoracotomy for carcinoma of the lung between 1973 and 1980, there were 177 patients older than 70 years. In this older group the major complication rate (major nonfatal and

Table 1. Final Histological Diagnosis

Diagnosis	Group 1	Group 2
Squamous	53%	51%
Adenocarcinoma	26%	16%
Large cell	16%	30%
Small cell	5%	4%

Table 2. Postoperative Staging

Stage	Group 1	Group 2
I	50%	56%
II	23%	14%
IIIa	27%	30%

Table 3. Hospital Mortality After Pulmonary Resection[a]

Age Group	Lobectomy	Pneumonectomy
1	1/53 (1.9%)	5/83 (6.2%)
2	1/21 (4.7%)	2/22 (9.1%)
Total	2/74 (2.7%)	7/105 (6.7%)

[a] There are no significant differences by χ^2 test.

death) was significantly higher in the older group (18%; 31/177) compared with those younger than 70 years (9%, 72/784) [9]. The more recent studies have only looked at the older population without the control of similar patients of younger age treated in the same unit [12]. The marked difference between these figures and those from the Lung Cancer Study Group of North America and our own probably reflects improved patient selection, anesthetic technique, and postoperative management. Indeed hospital mortality after pulmonary resection has steadily decreased since 1960 [8].

In the long term, our study shows that after 2 years there is an appreciable survival, with 62.3% of the younger patients and 72.5% of the older group still alive; this decreases to 50.0% and 66.6% after 4 years. Three major studies of long-term survival after pulmonary resection quote 5-year survivals of 27.0% [13], 30.0% [14], and 31.0% [11]. The increased survival in our group reflects our strict selection protocol, which rejects over 50% of patients referred for operation. This is supported by a study from Japan, using criteria similar to ours, that found an overall 5-year survival rate of 55% for patients older than 80 years [12].

Neither histological type nor pathological staging appeared to have an adverse effect on long-term survival in the older group compared with the younger patients; however, the numbers were small and no definitive statement should be made. In both groups there was a high incidence of stage III disease despite careful case selection; the overall incidence was 49/179 (27%). The Japanese Lung Cancer Study Group found 13 cases of stage IIIa disease in 33 patients (39%) older than 80 years who had undergone operation [12]. The routine use of mediastinal node dissection is known to unearth microscopic N2 disease [15], and this probably explains the higher incidence of stage IIIa disease in these two studies. It does not, however, seem to have had an adverse effect on the overall survival figures.

Table 4. Survival and Staging

	2-Year Survival		4-Year Survival	
Stage	Group 1	Group 2	Group 1	Group 2
I	77%	83%	66%	75%
II	61%	100%	53%	83%
IIIa	41%	53%	25%	40%

Table 5. Survival and Histology

	2-Year Survival		4-Year Survival	
Histology	Group 1	Group 2	Group 1	Group 2
Squamous	68%	59%	37%	36%
Adenocarcinoma	59%	86%	37%	67%
Large cell	70%	71%	68%	69%

The elderly patient with bronchial carcinoma who is not suitable for operation has a median survival of 7.7 months [11]. In this study the operative mortality of the elderly group was not markedly greater than that of the younger group, and the crude overall 2-year and 4-year survival was acceptable: more than 50% alive at 4 years. Therefore, it is our belief that no fit patient with carcinoma of the bronchus should be denied operation on the basis of age alone.

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References

1. Trends in cancer survival in Great Britain. London: Cancer Research Campaign, 1982.
2. Cancer Survival. OPCS Monitor 1988;MB1.88/1:5–5.
3. The Registrar General's Statistical Review for England and Wales, 1983–85. London: OHMS, 1986.
4. Hooper RG, Beechler CR, Johnson MC. Radioisotope scanning in the initial staging of bronchogenic carcinoma. Am Rev Respir Dis 1978;118:279–86.
5. Spiro SG, Goldstraw P. The staging of lung cancer. Thorax 1984;39:401–7.
6. Naruke T, Suemasu K, Ishikawa S. Lymph node mapping and curability at various levels of metastasis in resected lung cancer. J Thorac Cardiovasc Surg 1978;76:832–9.
7. Swinscow TDV. The chi-squared tests. In: Statistics at square one. 7th ed. London: BMA, 1983:43–53.
8. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty-day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 1983;86:654–8.
9. Nagasaki F, Flehinger B, Martini N. Complications in the treatment of carcinoma of the lung. Chest 1982;82:25–9.
10. Bates M. Results of surgery for bronchial carcinoma-patients aged 70 and over. Thorax 1970;25:77–8.
11. Kirsh MM, Rotman H, Bove E, et al. Major pulmonary resection for bronchogenic carcinoma in the elderly. Ann Thorac Surg 1976;22:369–73.
12. Shirakusa T, Tsutsui M, Iriki N, et al. Results of resection for bronchogenic carcinoma in patients over the age of 80. Thorax 1989;44:189–91.
13. Breyer RH, Zippe C, Pharr WF, Jensik RJ, Kittle CF, Faber LP. Thoracotomy in patients over seventy years. J Thorac Cardiovasc Surg 1981;81:187–93.
14. Thompson Evans EW. Resection for bronchial carcinoma in the elderly. Thorax 1973;28:86–8.
15. Goldstraw P, Kurzer M, Edwards D. Peroperative staging of lung cancer: accuracy of computed tomography versus mediastinoscopy. Thorax 1983;38;10–5.

Comparison of Hemodynamics and Ejection Fraction During Left Heart Bypass

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Temporary mechanical circulatory support during the postcardiotomy period has seen widespread application over the past 5 years. Recovery of sufficient cardiac function to allow removal of such support has usually been assessed by bedside hemodynamic variables during stepwise decrement of assist flows. To assess the efficacy of this approach and obtain prognostic information, 12 patients who required left heart bypass after coronary operations and who showed an indication of ventricular recovery, as evidenced by return of a pulsatile wave on arterial pressure tracing, were studied using blood pool radionuclide angiography during stepwise decrement of assisted flows. Hemodynamic variables (mean arterial pressure, heart rate, central venous pressure, pulmonary artery pressure, cardiac index, and systemic vascular resistance) did not correlate with survival during reduction of assist flows. Pulmonary artery pressure at maximum assisted flows and measured ejection fraction at flows of 60% or less of maximum flows correlated with survival; furthermore, if ejection fraction increased as assist flows were decreased, prognosis appeared excellent. Measurement of left ventricular ejection fraction during stepwise decrement of assisted flows in the postcardiotomy setting may provide valuable prognostic information and more clearly identify those patients who may be successfully separated from mechanical circulatory support.

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Approximately 1% to 2% of the patients undergoing a technically successful cardiac surgical procedure cannot be separated from cardiopulmonary bypass despite traditional inotropic support and intraaortic balloon counterpulsation [1]. Temporary mechanical circulatory support has gained acceptance and results using a variety of devices continue to improve. Once the patient is supported with a temporary device the usual approach has been to wean the patient from the device using readily available bedside hemodynamic criteria. Weaning protocols based on such criteria have been presented in the literature and are presently the standard of care [2, 3, Dixon CM, Rosenberg ID, Magovern GJ. Allegheny General Hospital clinical protocol for ventricular assist (personal communication)]. Experience using this weaning protocol when the Bio-Medicus pump (Bio-Medicus, Eden Prarie, MN) has been used for temporary left heart bypass in the postcardiotomy setting, at this center, has lead to unpredictable results. To achieve a more accurate index of left ventricular function and recovery, and to provide prognostic information, a weaning protocol based on noninvasive measurement of left ventricular ejection fraction has been established. The present report includes 4 patients previously included in a report in *ASAIO Transactions* [4], together with 8 new patients, and considers the prognostic value of left ventricular ejection fraction in patients who appear to be weanable from support by hemodynamic criteria.

Material and Methods

All patients who had undergone a technically successful cardiac procedure and who could not be weaned from cardiopulmonary bypass despite judicious use of inotropic agents and intraaortic balloon counterpulsation were considered candidates for further mechanical circulatory support. All patients were cannulated in the left atrium with outflow from the Bio-Medicus pump to the ascending aorta. While changing from cardiopulmonary bypass to left heart bypass, patients were not supported for a period of 15 to 45 seconds. Once left heart bypass was in place, volume status was adjusted to maintain flow to provide a cardiac index of 2.0 to 2.2 $L \cdot min^{-1} \cdot m^{-2}$. Heparin was reversed with protamine and hemostasis was meticulously achieved using blood and blood products as necessary. Inotropic agents were then slowly discontinued leaving patients on only 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine therapy. Intraaortic balloon counterpulsation was continued. Cannulas were brought out through the inferior aspect of the sternotomy incision and the incision was closed (sternum, fascia, and skin). Once the patient was in the intensive care unit, heparin administration was begun 6 to 12 hours after chest tube drainage had minimized. Patients were extubated as soon as feasible.

Ventricular recovery was assessed by temporarily decreasing pump flows and observing return of a pulsatile wave form on arterial line pressure tracing (other than that attributed solely to the intraaortic balloon pump).

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Table 1. Heart Rate and Mean Arterial Pressure During Weaning

Assist Flow (100% = 4 ± 1 L/min)	Heart Rate (beats/min) Survivors	Heart Rate (beats/min) Nonsurvivors	Mean Arterial Pressure (mm Hg) Survivors	Mean Arterial Pressure (mm Hg) Nonsurvivors
100%	100 ± 15	101 ± 12	87 ± 10	85 ± 10
41%–60%	110 ± 10	105 ± 15	85 ± 9	80 ± 11
≤24%	106 ± 11	110 ± 11	81 ± 10	79 ± 12

[a] p = not significant for all data points. Data are shown as mean ± standard deviation.

When evidence of ventricular recovery was seen (usually at 24 to 48 hours of support) a formal weaning trial was scheduled. These trials, performed in a fully anticoagulated state, consisted of a stepwise decrement in assisted flows by approximately 1,000 mL/min. At each step, heart rate, mean arterial pressure, pulmonary artery pressures, central venous pressure, cardiac index (measured by thermodilution cardiac output), and ejection fraction were recorded. Left ventricular ejection fraction was calculated by bedside computer-assisted blood pool radionuclide angiography as previously described [5]. Systemic vascular resistance was calculated at each level of flow.

Once the weaning trial was completed patients were returned to the operating room and the Bio-Medicus pump was removed. Inotropic support and intraaortic balloon counterpulsation were then adjusted to optimize hemodynamics.

Results

Twelve patients underwent the entire weaning protocol. Eight of these patients were ultimate (>30 days) survivors and 4 died soon (<30 days) after having their device removed. Average age of survivors was 61 years (range, 53 to 78 years) and that of nonsurvivors was 63 years (range, 53 to 71 years). Preoperative ejection fraction of survivors (0.40 ± 0.10) was not different than that of nonsurvivors (0.37 ± 0.12).

Table 2. Central Venous Pressure and Systemic Vascular Resistance During Weaning[a]

Assist Flow (100% = 4 ± 1 L/min)	Central Venous Pressure (mm Hg) Survivors	Central Venous Pressure (mm Hg) Nonsurvivors	Systemic Vascular Resistance ($dynes \cdot s^{-1} \cdot cm^{-5}$) Survivors	Systemic Vascular Resistance ($dynes \cdot s^{-1} \cdot cm^{-5}$) Nonsurvivors
100%	17 ± 4	18 ± 4	2,023 ± 345	2,062 ± 504
41%–60%	18 ± 5	19 ± 5	1,729 ± 280	1,877 ± 323
≤24%	18 ± 6	19 ± 5	1,710 ± 257	1,846 ± 510

[a] p = not significant for all data points. Data are shown as mean ± standard deviation.

Table 3. Pulmonary Artery Pressure and Cardiac Index During Weaning[a]

Assist Flow (100% = 4 ± 1 L/min)	Pulmonary Artery Pressure (mm Hg) Survivors	Pulmonary Artery Pressure (mm Hg) Nonsurvivors	Cardiac Index ($L \cdot min^{-1} \cdot m^{-2}$) Survivors	Cardiac Index ($L \cdot min^{-1} \cdot m^{-2}$) Nonsurvivors
100%	22 ± 4[b]	29 ± 3[b]	3.4 ± 0.4	2.6 ± 0.7
61%–80%	26 ± 6	29 ± 4		
41%–60%	24 ± 4	27 ± 5	3.1 ± 0.3	2.6 ± 0.6
25%–40%	26 ± 5	27 ± 11		
≤24%	28 ± 7	28 ± 5	2.9 ± 0.5	2.6 ± 0.8

[a] Data are shown as mean ± standard deviation. [b] $p < 0.05$ for survivors versus nonsurvivors; all other p = not significant for survivors versus nonsurvivors.

Heart rate, mean arterial pressure, central venous pressure, and systemic vascular resistance showed no significant difference in survivors and nonsurvivors as assist flows were decreased (Tables 1, 2). Mean pulmonary artery pressure in survivors (22 ± 4 mm Hg) was significantly lower than in nonsurvivors (29 ± 3 mm Hg) at 100% of assisted flows ($p < 0.05$) before beginning the weaning process (Table 3). This difference disappeared as assisted flows were decreased. Cardiac index was not significantly different in survivors and nonsurvivors at any percentage of assisted flows including flow rates of less than 25% of maximum (flows, 500 to 1200 mL/min) (see Table 3). Ejection fractions at greater than 60% of maximum assist flows were not different in survivors and nonsurvivors. Ejection fraction at 60% or less of maximum assist flows correlated with survival ($p < 0.05$) (Table 4). Ejection fraction at 60% or less of maximum flow was significantly better in survivors than ejection fraction at 100% of maximum flow. Ejection fraction essentially remained unchanged during decreased flows in nonsurvivors. Furthermore, 8 of 9 patients who displayed an increase in ejection fraction by a factor of 1.5 or greater at 60% or less of maximum assisted flow were long-term survivors (see Table 4).

The one patient in this latter category who did not survive died of a pulmonary embolism before hospital discharge while on a normal care ward. The 3 other

Table 4. Left Ventricular Ejection Fraction During Weaning

Assist Flow (100% = 4 ± 1 L/min)	Ejection Fraction (mean ± SD) Survivors	Ejection Fraction (mean ± SD) Nonsurvivors
100%	0.21 ± 0.09	0.17 ± 0.03
61%–80%	0.25 ± 0.04	0.14 ± 0.05
41%–60%	0.34 ± 0.09[a]	0.17 ± 0.05[a]
≤40%	0.33 ± 0.08[a]	0.18 ± 0.07[a]

[a] $p < 0.05$ for survivors versus nonsurvivors; all other p = not significant for survivors versus nonsurvivors.

SD = standard deviation.

patients died of multiorgan failure, which was the ultimate result of myocardial failure and low cardiac output after pump removal. In 2 of these patients this low flow state was characterized by increasing inotrope requirements 12 to 24 hours after device removal. This requirement eventually resolved after an additional 72 hours. The third patient experienced the abrupt onset of atrial fibrillation 6 hours after device removal with marked hemodynamic deterioration requiring emergent cardioversion. Cardiac output after cardioversion remained inadequate for several hours.

Comment

Pae and associates [6] and Pennington and co-workers [7] have shown that the functional status of the patients who have survived postcardiotomy cardiogenic shock is, for the most part, excellent. Pennington and co-workers have suggested that there may be a natural selection process whereby those patients with severely and irreversibly damaged myocardium either cannot be separated from their assist device or die soon after device removal. Evidence of ventricular ejection, ie, return of a pulsatile arterial wave form, during temporary decrease of assisted flows or evidence of ejection during maximum assisted flows is usually the earliest easily obtainable sign of ventricular recovery. In the past, stepwise decrement of assisted flows and monitoring of bedside hemodynamic variables has been the usual technique employed to assess feasibility of device removal. Using noninvasive measurements of ejection fraction appears to provide more prognostic information. If during such stepwise decrements in assisted flows the left ventricular ejection fraction increases (when left atrial cannulation is used) this seems to imply a good long-term prognosis; when ejection fraction remains unchanged or decreases, despite acceptable bedside hemodynamics, long-term prognosis appears poor.

Although not specifically studied, the method of calculating ejection fraction does not appear to be critical. Bedside transthoracic echocardiogram has been used to assess ventricular function in other postcardiotomy patients; although accurate, it appears to be technically difficult because of drainage tubes and sterile dressings. Transesophageal echocardiogram seems to overcome these technical difficulties and also gives an excellent indication of ventricular function. Echocardiography also appears to be a technique that can be used to assess right ventricular function; portable nuclear scanners have some difficulty with right ventricular imaging.

We have presently instituted a policy of waiting 6 to 12 hours after a weaning protocol is completed before removal of the assist device. During this period of time assisted flows are left at 15% to 20% of maximal flows (usually 500 to 1,000 mL/min) and hemodynamic variables are monitored. It is hoped that this will unmask those patients whose condition would deteriorate soon after device removal. Patients whose condition does display deterioration are supported at maximal assisted flows for an additional 48 hours. If no further evidence of recovery is seen, consideration is given to institution of more long-term circulatory support and evaluation for cardiac transplantation.

In conclusion, measurements of ventricular recovery by assessment of ejection fraction during stepwise decrement of assisted flow may provide valuable prognostic information that could guide subsequent therapy in the postcardiotomy patient.

References

1. Pennock JL, Pierce WS, Wisman CB, et al. Survival and complications following ventricular assist pumping for cardiogenic shock. Ann Surg 1983;198:469–78.
2. Adamson RM, Dembitsky WP, Reichman RT, et al. Mechanical support: assist or nemesis? J Thorac Cardiovasc Surg 1989;98(Suppl):915–21.
3. Magovern GJ, Golding LAR, Oyer PE, Cabrol C. Weaning or bridging. Ann Thorac Surg 1989;47:102–7.
4. Verani MS, Sekela ME, Mahmarian JJ, et al. Left ventricular function in patients with centrifugal left ventricular assist device. ASAIO Trans 1989;35:544–7.
5. Verani MS, Gaeta J, LeBlanc AD, et al. Validation of left ventricular volume measurements by radionuclide angiography. J Nucl Med 1985;26:1394–401.
6. Pae WE, Pierce WS, Pennock JL, Campbell DB, Waldhausen JA. Long-term results of ventricular assist pumping in postcardiotomy cardiogenic shock. J Thorac Cardiovasc Surg 1987;93:434–41.
7. Pennington DG, Bernhard WF, Golding LR, et al. Long-term follow-up of postcardiotomy patients with profound cardiogenic shock treated with ventricular assist devices. Circulation 1985;72(Suppl 2):216–26.

Late last year The Annals received an unsolicited editorial from Dr Richard M. Peters. So provocative were his thoughts that rather than publish his article without comment, we decided to ask several leading educators in our specialty to submit companion articles that address the problems posed by Dr Peters. Clearly the restructuring of cardiothoracic training for the future will require much thought and effort. We hope this Editorial Symposium will stimulate all of us to give a high priority to this critically important task.

Thomas B. Ferguson, Editor
John R. Benfield, Associate Editor, Editorials

Should We Care? Do We Care? What Should We Do?

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The length of cardiothoracic training is increasing. Is the quality correspondingly increasing or is the servitude just longer? Is the product better because of longer training or worse because the best and brightest are choosing other fields? Does it take 7 to 9 years to train a cardiothoracic surgeon or is the system flawed?

I believe servitude is rising but quality is deteriorating. We cannot think of cardiothoracic training only in terms of the last 2 years. We have a filter through which all cardiothoracic trainees pass in the general surgical programs. The quality, length, and attractiveness of the general surgery programs determine which medical school graduates enter and complete the first step of training. General surgery over at least the last 10 years has been moving down the list, behind orthopaedics, anesthesiology, radiology, and ophthalmology.

Should we care? The easy answer is the new generation wants an easier job so there is nothing we can do. This answer is as fallacious as the contention that children in inner city schools cannot be motivated to learn. There are too many examples of excellent programs disproving the fallacy of blaming the students as a reason for not restructuring the approach to teaching. We should insist on the restructuring for our trainees.

Should We Care?

The quality of general surgical training is deteriorating before our eyes. The first year consists of secretarial and messenger duties for the poorly managed hospitals with archaic information systems. The interns and house officers have been loaded with escalating needs for scheduling an increasing number of diagnostic and therapeutic procedures and providing most of the ever-increasing paperwork. At the same time the house officer does not participate in the preoperative evaluation and decisions but is called to provide a cursory history and physical examination to provide the paper trail for the same day admits. On many services they do not even have time to watch operations. Studies show that ¾ of their beeper's interruptions are unnecessary both during the day and night. Add to this our unwillingness to provide a reasonable call schedule.

Perhaps all this exploitation would be tolerable if they were learning to be surgeons by studying patients and then operating on them. The experience at all levels is becoming more a lesson in servitude to the hospital, attendings, and the system in general. Third party regulations require more paper and restrict activities that might enhance education. The faculties are grubbing for money; one of the results has been the move for areas of special competence in general surgery, leaving little for the 5- to 6-year residency.

Do We Care?

Unfortunately, there is little evidence of true concern for the primary purpose of residency—education. Examples are the unwillingness to cooperate with the thoracic resident matching plan and the lengthening of residencies to 3 years without criteria that can be audited to assure the purpose is education, not cheap assistants. Most important is our failure to recognize the importance of the deterioration of the filter, an education in general surgery appropriate to the needs of a future thoracic surgeon. If general surgery is 5 years of servitude necessary to get to cardiothoracic surgery training, we will miss the best and brightest.

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What Should We Do?

The future of cardiothoracic surgery depends on a constant infusion of new capable individuals into the specialty and all cardiothoracic surgeons should be guardians of this future.

Senior cardiothoracic surgeons have control of much of the decision-making apparatus but their actual experience as house officers was in a different world. Since the decision makers finished training the many technical advances have been accompanied by profound changes in the social structure of our society and the patterns of medical practice. Nostalgia and clouded memories must not block recognition that training programs must accommodate to these changes.

The more recent graduates and present residents must search their minds to find the things that did not serve the purpose of education but represented service to a poorly managed system. Catalogue these things and act responsibly as alumni for your training program and as members of the societies by becoming vocal advocates of improved training programs.

The major responsibility for change rests on the second and in some cases third generation of directors of cardiothoracic thoracic residency training programs. Theirs is the responsibility to make all changes locally that are feasible. Insist on modern information technology, and provide physician assistants and other ancillary help to provide support for tasks that do not need resident physician skill. Insist on a reevaluation of the entire educational sequence for cardiothoracic surgery. Are your clinical clerks getting attention so they become excited by problems of cardiothoracic surgery?

How can you make the general surgery filter less a block and more an asset to cardiothoracic training? How long should general surgery training be? Three, 4, or the present 5 to 6 years? What content should it have?

What should the content and the duration of the cardiothoracic portion of the residency be? Two or 3 years? How many coronary operations? What operative experience is needed in congenital heart disease? How is general thoracic surgery experience provided? Should separate tracks be available for general thoracic and cardiac concentration? What role for transplantation?

Those who care must use all of the influence that they have with the regulatory and certifying boards and in the committees of the various societies to develop a force to overcome the built-in inertia to change. Failure to achieve change will not be immediately apparent, but like the effect of smoking on coronary heart disease and lung cancer there is a long lag time. If we wait until the quality of trainees has deteriorated radical surgery will only be palliative at best.

Dilemmas in Cardiothoracic Surgical Education

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Dr Richard Peters' incisive editorial [1] raises pertinent questions about the troubled state of cardiothoracic surgical residency education today. The ramifications of the questions he raises are multitudinous, and only a few can be addressed in a limited space.

What General Surgical Education Does the Cardiothoracic Trainee Require?

The needs of the trainee relative to the two subdivisions of cardiothoracic surgery, cardiac and general thoracic surgery, are very different. The student of cardiac surgery needs a basic general education in surgery, to reiterate Dr Edward D. Churchill's pointed differentiation from an education in general surgery [2]. He or she requires broad comprehension of physiological and biochemical principles related to surgery, knowledge and experience in the complexities and complications attendant upon major surgery, and proficiency in basic surgical skills. He or she is then ready to embark, as are other single-organ surgeons—brain surgeons and eye surgeons—upon an educational program for the acquisition of the specialized knowledge—anatomical, pathological, and physiological, as well as the broad and complex spectrum of management problems and technical skills—that relate to cardiac surgery.

The trainee in general thoracic surgery must acquire additionally broad competence in the special fields of cervical surgery, gastrointestinal surgery, and vascular surgery. We are thus describing a complete training in general surgery as a prerequisite for general thoracic surgical education. I have long been convinced that an able and devoted candidate could easily be trained in general surgery in a 4-year period rather than the current 5-year requisite, given a rich enough milieu for training and a faculty dedicated to his or her education. This is not likely to happen for obvious reasons. Indeed, a problem now is to arrest the dilution that appears to be occurring in the content and depth of general surgical training.

See also page 807.

An alternative is to accept a briefer prerequisite training period from general surgical residencies and provide the necessary knowledge and training in skills during a cardiothoracic residency. This would inevitably require prolonging the latter, so there would be little or no net reduction in the length of post–medical school training for the cardiothoracic surgeon. With the present shortage of general thoracic surgical cases in so many of our cardiothoracic training programs, it seems impossible that many programs could provide this additional basic knowledge in surgery in addition to a mature training in the specialty itself. So many programs have difficulty at present in training their residents fully as cardiac *and* thoracic surgeons that to place an additional burden on them would be futile.

A last possibility, which is anathema to many in cardiothoracic surgery, would be to accept a shortened prerequisite in general surgical training (let us say, 3 years) and then have the applicants move directly to separate tracks in either cardiac surgical training or general thoracic surgical training. A small number of our cardiothoracic training programs could conceivably train individuals adequately in both areas, even with this shortened general surgical training, given a true commitment to the process. Anything less than that would erode even further the weakness of training in general thoracic surgery that already exists.

What Should Be the Content of a Cardiothoracic Surgical Residency Program?

As presently structured, the stated goal of the training program is to produce a *bona fide* specialist in cardiac and thoracic surgery. Both the American Board of Thoracic Surgery and the Residency Review Committee in Thoracic Surgery have accepted the fact that training in one area of cardiac surgery, congenital heart surgery, will be more of a general education than a preparation for immediate practice in the field. This is based fundamentally on the limited number of cases available for education and practice in the field. Specialization in that subdivision occurs by a process that, although not formally defined, works satisfactorily in practice, as Dr John Kirklin has pointed out in the past. We are all agreed that 2 years is the minimum time in which a competent candidate can acquire sufficient in-depth knowledge of the many problems of adult cardiac and general thoracic surgery, even in a program richly endowed with clinical opportunities. Necessary increases in the length of a program should depend on the resources of the local institution and their employment in education. We should not mandate increases in length of programs on undefined "general principles," seduced perhaps by the prospect of increased numbers of cardiothoracic residents that will result.

Unfortunately there is always tension in any training program between service and education. Case by case, service necessarily must take precedence over education once a trainee is involved in a case. In the broad picture, however, how the resident spends his or her training years should be determined on an educational basis.

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Specific questions that the director must decide on include: the number of months the trainee is assigned to cardiac and to general thoracic surgery; precedence of assignment to one type of patient or another in both cardiac (coronary artery bypass versus valvar surgery) and general thoracic surgery (esophageal versus pulmonary, for example). The flexibility to construct a program with educational purpose foremost must be maintained without compromising the care of patients. This means necessarily the assignment of general surgical residents and physicians' assistants to do additional work that must be accomplished by the clinical unit. No clinical unit can afford to pick and choose among its referred patients on the basis of educational merit, nor should this be done. This would deny our obligations and would quickly destroy our referral base!

The problem of adequate breadth of training is acute in different ways in both subspecialties of cardiothoracic surgery. In cardiac surgery, there is presently an overwhelming case volume of coronary bypass grafting. As I looked over the credentials of candidates for specialty examination a few years ago, I was adversely impressed by the huge percentage of their total training cases that was in this one single portion of the entire specialty. Although this might truly reflect what their practices would encompass, it certainly did not prepare them to be the broad specialists whom we label them to be when they are certified. The resident must be protected from becoming simply a technician for the accomplishment of coronary artery bypass grafting by paying attention to his or her assignments and to provision of adequate personnel. In general thoracic surgery, there are two problematic areas. First, the case load is often inadequate to train a general thoracic surgeon. Second, cases are maldistributed among the portions of the specialty, primarily between pulmonary and esophageal surgery. This situation is not analogous to that of congenital heart surgery, where patients are in short supply. *The cases are there.* The inadequate case load usually reflects lack of commitment on the part of the training program director and faculty to make a major effort to encourage this part of the specialty in their institution. The reasons are many—lack of interest, lack of properly trained faculty, unwillingness to divert facilities to this less remunerative area [3].

A good 10 months of assignment solely to general thoracic surgery, with a rich case load, is needed to prepare a resident adequately for a sophisticated practice of this subspecialty. A portion of this time should be spent as Chief Resident in the general thoracic surgical unit, carrying a maximally complex load of clinical and operative responsibility. There is, on the other hand, no shortage of cardiac experience.

There are alternatives to our stated but frequently uneffected goal of producing graduates competent in the broad range of general thoracic and cardiac surgery. These include frank subdivision of the two specialties. This could take a form like the Canadian certificate of special competence in general thoracic surgery, which produces specialists solely in that area, as Donald Paulson suggested [4]. Many benefits could result from such an option. Another alternative, consistent with the structure of cardiothoracic surgery in the United States and in most of Canada, is provision of special tracks that allow for a greater emphasis in one or the other of the areas. However, in a program with insufficient clinical cases and faculty devoted to thoracic surgery, such a curriculum could further impoverish the education of the trainee specializing in cardiac surgery. If we accept the likelihood that the basic structure and goals of our present training scheme are not likely soon to be altered, it becomes essential that we work at enriching the general thoracic case load of all training programs. Then we can actually begin to produce true cardio*thoracic* surgeons and not simply cardiac surgeons with a smattering of thoracic experience. Further, those few programs that have the capacity can provide a specialized track, producing graduates fully trained in both fields but with an enriched background in general thoracic surgery. Care must be taken not to minimize the cardiac training in such a program, because that would only give a mirror image of the widespread current sin of producing surgeons trained principally in coronary artery bypass grafting, a bit of valvar surgery, and a minimal acquaintance with pulmonary surgery.

I have not attempted to enumerate specific prescriptions for the cure of our educational ills. The first steps toward resolution are heightened awareness of their existence and analysis of their nature—such as that provided by Dr Peters in his editorial—and, most of all, *commitment* to our educational role. Such commitment is always piously applauded. It requires, however, devoting a great deal of time, of energy, and—it cannot go unmentioned—of finances. The last derives from the need to provide additional personnel to handle cases not appropriately included in the residents' burden and to provide facilities and faculty to broaden the program's depth and breadth. Another benefit to renewing our commitment will be the infection of medical students participating in cardiothoracic surgical electives, general surgical residents rotating through the service, and our own cardiothoracic surgical residents with renewed enthusiasm for an exciting and rewarding area of surgery. Unfortunately, I share Dr Peters' concern that this commitment is often sadly lacking, as witnessed by the unwillingness of thoracic residency directors to support a resident matching plan universally agreed to be of benefit to the trainee, and also, as he pointed out, by the extension of the length of training programs without a corresponding increase necessarily in quality of training.

Because the invitation to prepare this editorial suggested that I describe our own institutional approaches, I shall close with a brief description of salient features of our program at the Massachusetts General Hospital. Experience has shown that cardiothoracic trainees may change their ultimate practice goals as their training proceeds. Whether their goals are in cardiothoracic, thoracic, or cardiac surgery, we have endeavored to provide the two trainees a year with a full, in-depth training in both subspecialties. With regret, we recently extended the program to 2½ years to accommodate the need for more comprehensive training in congenital heart surgery, with the cooperation of our sister institution, Boston Children's Hospital. Each resident receives from 10 to 14 months of training in general thoracic surgery and 16 to 20 months of cardiac training (adult and congenital), and every resident serves 6 months each as Chief Resident in the Cardiac Surgical and the General Thoracic Surgical Units. These tours occur in the final 18 months of tenure. The variation in division of training months depends on the individual's interests in each subspecialty. Residents begin major operating immediately, on the assumption that they have already had not only a complete general surgical training but a basic introduction at least to endoscopic techniques and minor cardiothoracic surgical procedures.

Within the bounds of necessary obligations for care of patients with particularly difficult problems, the Chief Resident is encouraged to operate on a particular day on a case that provides maximum value in his or her educational program. Obviously, such a program requires coequal cardiac and general thoracic units that have sufficient critical mass of cases, dedicated faculty, geographically separate nursing units and intensive care facilities, service-assigned operating rooms or times, separate residents assigned without call obligations from the other unit, and an organized educational conference program with fully developed relationships with corresponding affiliated specialists in each field.

In the last decade this program has produced 5 graduates who devote themselves wholly to cardiac surgery, 6 who practice both cardiac and thoracic surgery in varying proportions, and 5 who are wholly committed to general thoracic surgery (1 graduate left the specialty for medical reasons, another is in the armed forces). This description is not presented as an ideal solution to cardiothoracic educational problems. However, it does offer an example of one model that, consistent with present formal requirements, attempts to fulfill national needs for cardiac and thoracic surgical specialists in what we hope is a rational way.

References

1. Peters RM. Should we care? Do we care? What should we do? Ann Thorac Surg 1991;51:807–8.
2. Churchill ED. General education in surgery. Ann Surg 1956; 144:506–8.
3. Grillo HC, Benfield JR, Faber LP, et al. General thoracic surgery in cardiothoracic surgery. The search for balance. J Thorac Cardiovasc Surg 1984;88:321–3.
4. Paulson DL. A time for assessment. J Thorac Cardiovasc Surg 1981;82:163–8.

Training for Cardiac Surgery in Children and Adults

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Dr Peters' editorial [1] addresses issues of enormous importance to the future of cardiac surgery for children and adults in the United States. Two facts emphasizing the importance of these issues are (1) the 2 years of training required by the American Board of Thoracic Surgery in the 1950s remain the same today, even though the large activities of cardiac surgery and pulmonary transplantation, to name just two, did not even exist at that time, and (2) the United States is one of the few countries in the developed world in which cardiac surgical trainees are required to spend 5 years in general surgery before entering cardiothoracic training.

One cannot contemplate training in cardiac surgery without first contemplating the nature, or content, or scope of cardiac surgery itself today. Cardiac surgery includes the coronary artery bypass graft operation for arteriosclerotic coronary artery disease, and operations for repair of ischemic left ventricular aneurysm, ischemic mitral incompetence, and postinfarction ventricular septal defect; the repair, and the replacement, of diseased aortic, mitral, and tricuspid valves; the repair of a large number of different kinds of congenital heart disease, including particularly the methodology of doing this in neonates and infants; the surgical treatment of medically intractable cardiac tachyarrhythmias, including the Wolff-Parkinson-White syndrome and other supraventricular tachycardias, atrial fibrillation, and ventricular tachycardia; the removal of various types of cardiac tumors; the repair of a wide variety of types of cardiac trauma; the repair of acute and chronic dissections and aneurysms of the ascending aorta, arch, and descending thoracic aorta; and the removal of acute and chronic pulmonary emboli.

See also page 807.

In addition to these operations, the cardiac surgeon is expected to have learned the pathophysiological basis and technical details of cardiopulmonary bypass and its closed chest counterpart, extracorporeal membrane oxygenation; profoundly hypothermic total circulatory arrest; the management of the myocardium itself during operation; left ventricular, right ventricular, and biventricular assist devices; cardiac transplantation; intensive care of neonates, infants, children, and adults after cardiac operations; and the in-hospital postoperative care of patients after all these kinds of cardiac surgical procedures, including antibiotic, anticoagulant, and antiplatelet therapy and antiarrhythmic therapy.

This rather boring recital of the nature of modern cardiac surgery is absolutely necessary as emphasis of the complete impossibility of acquiring the necessary information and skills within a 2-year period shared with general thoracic surgery. Even the basic manipulative surgical skills required for cardiac surgery must be learned, or unlearned, or relearned during the cardiothoracic residency. How many times have we all found it necessary to reteach knot-tying to a recently "graduated" general surgeon?

We all know that the probabilities are small that the duration and nature of training for cardiac surgery in the United States can be changed, but the potential for deterioration of the specialty in the United States without it, and the somewhat selfish nature of the forces aligned against it, suggest strongly that we should continue and indeed accelerate discussion of it. The changes should include at least ablation of the requirement that full certification by the American Board of Surgery is a prerequisite to certification in cardiothoracic surgery, reduction of the general surgery minimal time requirement to 3 years, and enlargement of the minimal cardiothoracic surgery time requirement to 3 general years plus 1 specialty year. The specialty year should be in a center specifically identified for advanced training in general thoracic surgery (and no doubt other more specialized areas within this discipline); surgery of ischemic heart disease; valve surgery; arrhythmia surgery; aortic surgery; surgery for congenital heart disease; cardiac and pulmonary replacement surgery, including transplantation; and probably other special areas as well.

These considerations pertain only to providing the trainee with current techniques and current knowledge, but they do not necessarily provide him or her with the techniques and motivations for absorbing the new techniques and knowledge that will surely develop during his or her 30 or so years of life as a cardiothoracic surgeon. Generally these have been informally provided by faculty persons and other teachers seriously interested in the continued growth of the trainee, and the time necessary for this is an added reason for lengthening the training period in cardiothoracic surgery itself. Actually, this informal method for teaching the trainee is quite suboptimal, and time should really be provided to the trainee for learning the essential features of evaluating published papers and lectures, including very specific instruction

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and experience in performing and interpreting the statistical analyses so necessary in the modern world.

So far, this proposal has provided no time or incentive to the cardiothoracic surgical trainee to develop new knowledge. This gap is potentially fatal to the appropriate future development of cardiothoracic surgery. It is also wasteful of the talents of many of the young people who enter into cardiothoracic surgery. Likewise, it robs those who might be interested of the excitement of learning the methods appropriate to defining problems and designing experiments and trials for solving them. One year is an absolute minimum to begin the development of skills in this area. The usual "year in the lab" is not what is envisioned in this recommendation, but rather a far more intense period under the direct leadership and tutelage of an experienced investigative cardiothoracic surgeon or clinician in an allied area. A period of time in a truly basic science is always advantageous, but few trainees in cardiothoracic surgery are equipped to take full advantage of such an opportunity.

The current attachment to the status quo in the training of cardiac surgeons comes at a time when, in my opinion, the field of cardiac surgery will soon be recognized as being overpopulated. The decline in the prevalence of younger patients undergoing coronary artery bypass grafting, for example, may be as much due to the reduced prevalence of new cases of ischemic heart disease (brought about by unknown epidemiologic factors, as well as a markedly changed lifestyle in the United States) as it is to percutaneous transluminal coronary angioplasty. If this is true, it will be only a few more years until not even the elderly will be "available" in large numbers for the coronary artery bypass operation. The prevalence of rheumatic fever has been radically reduced, and consequently so has mitral valve disease. Congenital heart disease is more and more requiring only a single operation, and that generally performed in early life. Thus the need for large numbers of practitioners of cardiac surgery is probably declining while the need for highly trained, unusually competent, focused and yet innovative cardiac surgeons is increasing. Witness the rapid development of cardiac transplantation, and the coming impact of genetic manipulation of cells on the discipline of cardiac surgery. The suggested changes in the training programs are, among other things, adaptations to these changing times and changing needs.

Thus, I have great sympathy with Dr Peters' editorial. Hopefully it will perturb the system sufficiently that open and honest attention will be given to it at all levels, and perhaps especially by chairmen of departments of surgery and directors of cardiothoracic surgical programs.

Reference

1. Peters RM. Should we care? Do we care? What should we do? Ann Thorac Surg 1991;51:807–8.

General Thoracic Surgery—Issues and Direction

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General thoracic surgery in the United States is a complex, multifaceted issue both for the specialty of thoracic surgery as a whole and, even more important, for patients who require extracardiac thoracic operations. The controversy involves (1) the very definition of thoracic surgery, (2) the proper place of general thoracic surgery in thoracic surgery training programs, and (3) ensuring the future survival of general thoracic surgery within the specialty of thoracic surgery. At one extreme are the *cardiac* surgeons, who perform virtually no general thoracic surgery in their practices. They see no "issue" regarding general thoracic surgery, do not want to hear about it, and would prefer it if the specialty of "thoracic" surgery were renamed "cardiac" surgery and general thoracic surgery simply went away, either to become a separate specialty or to be absorbed by general surgery. At the opposite extreme are the *thoracic* surgeons—the "chest" surgeons—zealously committed to pulmonary and esophageal surgery, expressing indignation at being viewed as "second class citizens" by cardiac surgeons, whom they view as competitors for operating room time, intensive care, and hospital beds, and utilization of thoracic surgery resident manpower. The practice of cardiac surgery has no relevance to their professional lives. They would like to see the current required 2-year cardiothoracic surgery residency reduced to 1 year of general thoracic surgery training with a separate certificate of competence in this specialty, thereby eliminating cardiac surgical experience from the training of future general thoracic surgeons. Between these two extremes are permutations as varied as the program directors practicing cardiac, general thoracic, or cardiothoracic surgeons who espouse them. The entire matter is further confounded by a general lack of awareness of where the current impetus for reviewing the issue of general thoracic surgery has originated and the appropriate roles of the American Board of Thoracic Surgery, the Residency Review Committee for Thoracic Surgery, and the Liaison Committee of the American Association for Thoracic Surgery (AATS) in this matter. It is the intent of this communication to review and clarify some of these issues and to discuss some future proposed directions.

See also page 807.

It was Dr Donald Paulson's 1981 Presidential Address to the American Association for Thoracic Surgery entitled "A Time for Assessment" [1] that called attention to the secondary role of general thoracic surgery in our specialty, which had resulted from the tremendous technological advances in cardiac surgery since the early 1950s. He expressed his concern and that of several other leaders in thoracic surgery that the preponderance of cardiac surgery, particularly myocardial revascularization operations, in the majority of our training programs was producing "cardiac surgeons" with minimal training or interest in general thoracic surgery. The inevitable result, already occurring at that time, was that the overall quality of general thoracic surgical care in this country would suffer as pulmonary and esophageal surgery was performed by surgeons with minimal thoracic training.

The Council of the AATS responded to Dr Paulson's recommendation by appointing the Liaison Committee for Thoracic Surgery, charged with maintaining unity in the overall specialty of cardiothoracic surgery, thereby enhancing better health care delivery, by preserving an appropriate balance of training in the respective components of our field. During the past 9 years, the Liaison Committee has discussed and debated various alternatives for fulfilling its mandate—ensuring that general thoracic surgery is properly represented in the curriculum of our training programs and preserving the integrity of the specialty of thoracic surgery. Through a series of questionnaires to thoracic surgery program directors (1983, 1986, 1989), the Liaison Committee has repeatedly confirmed the impression that general thoracic surgical training is not optimal in many of our programs.

In its most recent (December 1989) polling of thoracic surgery program directors (107 of 109, or 98%, responding), the Liaison Committee again documented that discussion alone about the means for improving the quality of general thoracic surgery training has been insufficient to effect change. A given body of knowledge is best transmitted to others by individuals particularly interested in the field and dedicated to teaching it. Yet, in 1986, 20% of training programs lacked designated faculty with a primary clinical interest, responsibility, and residency teaching assignments in general thoracic surgery; now, 4 years later, 21% do. Twenty-nine percent (31) of our thoracic surgery program directors indicate that they currently have an available general thoracic surgery faculty position, and nearly 50% anticipate the availability of such a position within the next 3 to 5 years. Most educators agree that a subject is best learned by giving students the opportunity to concentrate on this area for a dedicated period of time, encumbered as little as possible by other obligations and distractions. Yet, in 1986, only 52% of programs provided "pure" general thoracic surgery rotations for their residents; now 49% do. The Liaison Committee has recommended a minimum of 6 months of designated general thoracic surgery training

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within the "ideal" 24-month thoracic surgery residency training program. Although fully acknowledging that this represents an ideal, only 64% of directors report that their trainees receive 6 months or more of general thoracic surgery training during their 2-year clinical experience.

It is naive to think that the solution to this problem is so simple as having the American Board of Thoracic Surgery (ABTS) or the Residency Review Committee for Thoracic Surgery issue edicts that redefine the specialty of thoracic surgery and hence the body of knowledge to be encompassed by only certain of our training programs providing access to separate certificates of competence in general thoracic surgery or cardiac surgery alone. Specialty boards exist to protect the public by providing assurance that a certified medical specialist has successfully completed an approved educational program and an evaluation process, including an examination designed to assess the knowledge, experience, and skills requisite to the provision of high-quality patient care in the specialty. The ABTS has representation from the AATS, The Society of Thoracic Surgeons, the American Surgical Association, the American College of Surgeons, the American Medical Association, and the American Board of Surgery, and it is a *certifying* or credentialing organization for our specialty, as defined above. Since its inception as a primary Board in 1971, the ABTS has established qualifications for examination and procedures for certification and recertification of individual physicians who have trained in programs approved by the Residency Review Committee for Thoracic Surgery. In its annual Booklet of Information the Board states that "training in both general thoracic surgery and cardiovascular surgery is an essential part of any approved program no matter what area of thoracic surgery a candidate may choose for his/her practice" [2]. The scope of the specialty of thoracic surgery, according to the Board, "encompasses a knowledge of the normal and pathologic conditions of both cardiovascular and general thoracic structures. This involves congenital and acquired lesions (including infections, trauma, tumors, and metabolic disorders) of both the heart and blood vessels in the thorax, as well as diseases involving the lungs, pleura, chest wall, mediastinum, esophagus, and diaphragm. In addition, the ability to establish a precise diagnosis, an essential step toward proper therapy, requires familiarity with diagnostic procedures such as cardiac catheterization, angiography, electrocardiography, conventional radiologic studies, computerized tomography and imaging techniques, endoscopy, tissue biopsy and biologic and biochemical tests appropriate to thoracic diseases" [3]. The Board continues to examine in all areas of our specialty—adult and pediatric cardiac surgery as well as general thoracic surgery. Residency review committees (RRCs) are accrediting organizations that function under the auspices and authority of the Accreditation Council for Graduate Medical Education. Each RRC has its parent or sponsoring organizations, in the case of thoracic surgery, the ABTS, the American Medical Association Council on Medical Education, and the American College of Surgeons. The RRC for a particular specialty develops special requirements for training programs in that specialty. These special requirements are reviewed by the RRC's sponsoring organizations, and if approved by the Accreditation Council for Graduate Medical Education, define the requirements for "the essential educational content, instructional activities, patient care responsibilities, supervision, and facilities that should be provided by the programs in the particular specialty" [4].

The Special Requirements for Residency Training in Thoracic Surgery [5] defines a thoracic surgery residency as a "graduate education program designed to give the resident a broad clinical experience in pulmonary, esophageal, mediastinal, chest wall, diaphragmatic and cardiovascular disorders. The residents, on completion of the program, are expected to be clinically proficient in these areas as well as knowledgeable in the use of cardiac respiratory support devices."

Thus, the specialty of thoracic surgery, as defined by its own certifying Board and accrediting RRC, includes general thoracic as well as cardiovascular disease. And despite the existence of this established definition, the specialty itself has been inconsistent and has contributed to division within its own ranks by allowing the very term *thoracic surgery* to have varied meaning. Thus for many, there are the *cardiac* surgeons and the *thoracic* surgeons, those who perform general thoracic surgery. One of our two major journals—the *Journal of Thoracic Surgery*—was renamed in 1959 the *Journal of Thoracic and Cardiovascular Surgery*, an obvious statement that the term *thoracic surgery* was not felt to adequately reflect the scope of this specialty. Yet, the name of our specialty Board has remained since its inception the American Board of *Thoracic Surgery*.

Some would argue that the emergence of cardiac surgery as a highly specialized and technologically sophisticated field justifies a separate specialty Board and residency training program. Why insist that cardiac surgeons be trained in general thoracic surgery or general thoracic surgeons in cardiac surgery when these fields are so clearly divergent in scope, technique, and practice? Should we not face the reality that cardiac surgery, performed by the majority of thoracic surgeons now seeking board certification, is already completely divorced from general thoracic surgery? If history has value and the wisdom of our forefathers merits reflection, we should ask ourselves if there is reasonable rationale for preserving the integrity of thoracic surgery by continuing to require residency training and certification in both cardiac and general thoracic surgery. I believe that there is. From the very beginning of our formal educational process, we are required to study subject matter that we will not use per se in our ultimate professional lives. Be it algebra, art history, music appreciation, or anthropology, these subjects are valued by educators as a foundation for later intellectual achievement. In our medical schools, curricula encompass psychiatry and medical history. Should these not be taught to budding surgical residents? Our general surgery residencies include rotations in obstetrics and gynecology, orthopaedics, and neurosurgery. Are these useful for a future thoracic surgeon? We are all constantly reminded that we have forgotten more than we have learned along the road to our ultimate careers as thoracic surgeons. But to fail to expose to basic concepts in both cardiac and general thoracic surgery those being trained to carry on our profession is to weaken the final product on which the specialty depends for its survival. The "better," ie, more broadly trained cardiac surgeons are able to manage the occasional postoperative organized fibrohemothorax, the bronchogenic carcinoma occurring concomitantly in a patient requiring coronary bypass grafting, and the persistent air leak following mechanical ventilation after a cardiac operation. A cardiac surgeon may not perform antireflux operations in his or her practice, but he or she should understand that the patient with reflux esophagitis, exacerbated by the supine position after coronary bypass grafting, may have chest pain of noncardiac origin and require a diagnostic and treatment plan that does not involve a cardiac catheterization laboratory. Conversely, general thoracic surgeons rely heavily on cardiac surgical training in the perioperative monitoring of their patients, intrapericardial resections of lung tumors, dissecting esophageal cancers that are involving the pericardium, treatment of traumatic aortic rupture, and now lung transplantation. It seems extraordinarily short-sighted and narrow-minded to argue for separate specialties of cardiac and general thoracic surgery when common sense tells us that organs that share the anatomical proximity of the heart, aorta, lungs, and esophagus are meaningfully related in the treatment of many diseases that affect them.

Perhaps the most important question we should be asking ourselves is, will patients being operated on by either cardiac or general thoracic surgeons lacking formal training in a totality of their specialty have the same quality of care that has been characteristic of American thoracic surgery from its inception? The answer is no. Thus, the founders of our specialty have defined the scope of thoracic surgery and the mechanism that has been put in place by its Board to certify thoracic surgeons. The majority of the leadership of American thoracic surgery has been committed over the years to the concept of thoracic surgery as a whole, both its cardiac and general thoracic components. There *is* no current option for being certified as either a cardiac or a general thoracic surgeon alone, because there exist no separate certifying mechanisms, and there is currently no intention of establishing them. One has only to participate in the activities of either the ABTS or the RRC to appreciate the complexities of a fair certification and accreditation using the established definition of thoracic surgery. To fragment these efforts by requiring assessment of credentials or training in either cardiac or general thoracic surgery would create tremendous additional problems for both the ABTS and the RRC that could not be managed by the existing organizational structure now in place. The prevailing opinion of the ABTS and the RRC for Thoracic Surgery is that the integrity of the specialty of thoracic surgery should be maintained. And at the present time, *there is a problem in our specialty with regard to general thoracic surgical training.*

As indicated above, the Liaison Committee for Thoracic Surgery was established by the Council of the AATS because thoracic surgery leadership at the time perceived a growing imbalance between cardiac and general thoracic surgery training, availability of case material, accessibility to hospital resources (operating time and beds), and research support. The Committee lacks authority per se but has functioned in an advisory capacity reporting annually to the AATS Council its recommendations. Editorials reviewing these recommendations have appeared in our journals [6–8] and have attempted to keep the cause of general thoracic surgery alive. The members of the Liaison Committee, all thoracic surgery program directors and educators themselves, have made earnest effort over the past 9 years to focus on educational objectives aimed at preserving the integrity of the specialty of thoracic surgery—*both* its cardiac and general thoracic divisions. Its "recommended guidelines for general thoracic surgery training within a cardiothoracic training program" include at least 6 months of concentrated exposure to general thoracic surgery training within the standard 2-year residency; an operative experience providing a minimum number of indexed cases, as well as preoperative and outpatient evaluation; and an appropriate general thoracic surgery conference schedule [8]. The spirit of these recommendations is to provide a guide for program directors for assessing the adequacy of their residency training in this area and *not* to impose a rigid set of regulations that prevent program directors from being imaginative and innovative. At its May 1990 meeting, the Council of the AATS endorsed these recommendations and forwarded them to the RRC for Thoracic Surgery for consideration. At its July 27, 1990, meeting, the RRC discussed the recommendations of the Liaison Committee, and as a result of its deliberations decided that the following statement from the Liaison Committee and the AATS will be included in the Special Requirements when they are revised: "Every accredited [thoracic] surgical training program in the United States should have at least one designated cardiothoracic faculty member responsible for coordinating multidisciplinary clinical conferences and organizing instruction and research in general thoracic surgery." The ABTS plans to continue to examine candidates in general thoracic as well as cardiac surgery. So long as the definition of thoracic surgery includes *both*, the mission of our residency programs must be to provide adequate training, as defined by the RRC, in both areas. Hopefully by requiring that someone in every program at least be responsible for teaching general thoracic surgery, the overall quality of our training programs will be improved.

But there is currently a serious problem before us—the shortage of qualified surgeons practicing general thoracic surgery. At a number of community hospitals, privileges to perform pulmonary and esophageal operations are being granted to surgeons with minimal thoracic surgery training and experience. The Liaison Committee is convinced that if the integrity of the specialty of cardiothoracic surgery is to be maintained, the most important task before us is to produce a new generation of academic general thoracic surgeons both to better train our cardiothoracic residents and to serve as role models and catalysts for research endeavors for residents interested in pursuing this subspecialty. A few programs with the ambition *and* resources—clinical, research, and faculty—to produce *academic* general thoracic surgeons are attempting to do so. For example, at the University of Michigan, residents completing the 2 standard years of cardiothoracic surgery residency and wishing to pursue a career in academic general thoracic surgery are being offered an optional third year of fellowship training—an apprenticeship in clinical general thoracic surgery with basic science laboratory experience as well, to facilitate their transition to a faculty position. At Barnes Hospital, on the other hand, thoracic residents choosing a career in general thoracic surgery are being offered a general thoracic surgery "track" with a preponderance of training in this subspecialty while still providing the minimum cardiac experience for Board certification. Other formulas for achieving the same end are certainly possible within the existing requirements of the RRC, which allows the current 2 years of required residency training to be interrupted by up to 2 years for specialized training in an area of the candidate's interest.

Many of our traditional cardiothoracic surgery residency training programs have been training residents in general thoracic surgery for years. Given the existing preponderance of cardiac surgery in most of our residency programs as well as the remunerative incentives of cardiac surgery, however, few residents in recent years have opted for careers as general thoracic surgeons. And even fewer have selected careers as *academic* general thoracic surgeons. There are not enough role models to guide them in this direction. Our specialty must replenish its ranks of teachers of general thoracic surgery, and that translates to more academic general thoracic surgeons from our training programs.

Based on the data from its 1989 questionnaire, the Liaison Committee established in the AATS central office a directory of available academic general thoracic surgery faculty positions, both to allow residents to see the number of job openings available to them in this field and to facilitate their obtaining these positions. Unfortunately, preliminary feedback to the Liaison Committee has indicated that a number of the listed available general thoracic surgery faculty jobs come with little or no commitment by the respective thoracic surgery divisions or departments to developing strong general thoracic programs. The applicants are invited to "build up general thoracic surgery" without being offered a commitment for designated operating time or hospital beds, dedicated resident rotations, or salaries competitive with junior faculty recruited to perform cardiac surgery. This must change if the specialty is to survive intact. The presence of teachers of general thoracic surgery in every thoracic surgery residency is an achievable and realistic goal. Intelligent residents pursuing careers in thoracic surgery seek training programs that offer experience and education in the *entire* field in which they will some day seek certification. *Balance* in cardiac and general thoracic surgery is an asset to every program.

The Liaison Committee will continue to examine the teaching of general thoracic surgery in our training programs. It will update the roster of available academic general thoracic surgery positions in the country and make this list available to residents in training. It will seek to develop guidelines to assist current training programs that are interested in developing general thoracic surgery "tracks." It will no doubt take several years before it is more widely accepted that (1) general thoracic surgery is a viable and exciting career pathway and (2) there *are* available training programs where interested thoracic surgery residents can obtain intensive experience in this field before launching their careers as general thoracic surgeons. The issue of general thoracic surgery is really a combination of issues for the entire specialty of thoracic surgery. General thoracic surgery has *not* been "lost to general surgery." The number of qualified American surgeons now performing complex general thoracic operations is inadequately and dangerously low. Patients requiring tracheal resections and reconstruction, bronchoplasties, segmental pulmonary resections, lung transplantations, chest wall resection and reconstruction, treatment of empyemas, esophageal resections, management of esophageal neuromotor dysfunction and reflux, and treatment of mediastinitis or mediastinal tumors are best treated by surgeons who have appropriate training in these areas, not a casual exposure to thoracic surgery as evidenced by a few pulmonary or esophageal resections in a general surgery training program. In its enthusiasm to develop the exciting area of cardiac surgery, thoracic surgery as a specialty has neglected general thoracic surgery, which has always been its foundation. It is time to get back on track and strike the balance that Dr Donald Paulson talked about in 1981. We should commit as a specialty to developing a new generation of general thoracic surgery faculty who will in turn train new general thoracic surgeons to maintain the high standards of care for our patients that has always characterized American thoracic surgery.

References

1. Paulson DL. A time for assessment. J Thorac Cardiovasc Surg 1981;82:163–8.
2. The American Board of Surgery, Inc. Booklet of Information. Office of the Board. Evanston, IL, January 1990:10.
3. Clinical Competence in Thoracic Surgery. Guidelines for Hospital Privileges for Thoracic Surgeons. American Board of Thoracic Surgery, October, 1984.
4. Directory of Graduate Medical Education Programs. Requirements for accreditation of programs. American Medical Association, Chicago, IL, 1988:11.
5. Directory of Graduate Medical Education Programs. Essentials of Accredited Residencies. American Medical Association, Chicago, IL, 1988:106.
6. Grillo HC, Benfield JR, Faber LP, et al. General thoracic surgery in cardiothoracic surgery: the search for balance [Editorial]. J Thorac Cardiovasc Surg 1984;88:321.
7. Grillo HC, Benfield JR, Faber LP, et al. General thoracic surgery in cardiothoracic surgery: the search for balance [Editorial]. Ann Thorac Surg 1984;38:427.
8. Orringer MB, Cooper JD, Magovern G, et al. The continuing dilemma of general thoracic surgery—where to now? J Thorac Cardiovasc Surg 1989;97:649.

Thoracic Surgery Training: It Is Time for a Change

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Dr Peters' provocative editorial [1] emphasizes the need to restructure residency training for thoracic surgeons. The primary issue faced by educators and program directors is the ability to educate thoracic surgeons who will advance the quality of patient care and increase knowledge in the specialty. Dr Peters proposes to shorten the general surgery training required for thoracic surgery. He points to the deterioration in the operative experience in these programs, indicating that thoracic surgery programs must take up the slack. There are additional compelling reasons for increasing the length of thoracic training programs.

See also page 807.

The changing character of cardiac and general thoracic surgical practice mandate restructuring with shortening of the general surgery training period. Training in general surgery provides necessary background and skills for the thoracic surgeon, which can be acquired in 3 or 4 years. However, both cardiac and general thoracic surgery are increasing in complexity and require more training in depth. This can be accomplished logically by increasing the time devoted to specialized training. Recent progress in thoracic oncologic surgery is an example of the complex evolution of our specialty. Thoracic oncologic surgery is the mainstay of contemporary training in general thoracic surgery because of the high incidence of lung cancer. The thoracic surgeon treating lung cancer must have experience with complex operative procedures including sleeve resection, tracheoplastic and bronchoplastic procedures, resection and repair of the great vessels, intrapericardial pneumonectomy, and radical mediastinal lymph node dissection. Effective management of esophageal cancer requires competency in at least four operations including Ivor-Lewis esophagectomy, total intrathoracic esophagectomy with anterior cervical anastomosis, transhiatal esophagectomy, and colon interposition. Extensive experience in operations involving the mediastinum, chest wall, and pulmonary metastases is necessary for adequate training.

Operative skills alone are not enough. The management of virtually all thoracic oncology patients now requires multidisciplinary approaches. The thoracic surgeon must be familiar with indications and timing of chemotherapy and radiation therapy. The effect of these modalities on surgical complications and outcome must be evaluated with prospective clinical trials conducted by surgeons. The thoracic surgeon must be trained to function as the patient's primary physician with the ability to actively participate in and coordinate treatment. This takes time and commitment by faculty.

It is time to reexamine the current requirements for entry into a thoracic residency program including completion of a chief residency year in general surgery. The requirement for being double-boarded both adversely affects the training of the general surgeon as a specialist and unnecessarily prolongs the thoracic residency program by an additional 1 or 2 years. Specifically, we would recommend that the thoracic training programs and the American Board of Thoracic Surgery accept residents after completion of either 3 or 4 years of a general surgery residency. Thus, the board requirement for a chief resident (PG-5) year and certification in general surgery would be eliminated. This would also benefit the specialty training of the general surgeon, because the chief resident going into general surgery would have more access to the operative experience and management of complex patient diseases involving their specialty areas, such as liver, pancreas, vascular, and pelvis surgery, that are not germane to the training of a thoracic surgeon.

What advantages would such a proposal have for thoracic training? First, it would reduce the overall training by 1 to 2 years. Second, it would permit the addition of a third year of thoracic training without the added burden of lengthening the entire training process. This may, in turn, allow for more in-depth training of individuals, especially in areas of multidisciplinary cancer treatment for lung and esophageal cancer and cardiac transplantation. Third, it avoids the required training in general surgery areas that are less relevant (or even irrelevant) to the preparation of surgical technique and patient decision-making for thoracic surgery. What benefit is there, for example, of requiring a thoracic surgeon to understand the options for multidisciplinary breast cancer, or rectal cancer treatment, surgical management for pancreatic or inflammatory bowel disease, or a modified neck dissection for thyroid carcinoma?

Are there any disadvantages? Some have stated that the requirement for 5 years of general surgery training allows for a greater process of professional and personal maturation. However, this may not be a valid concept and may be counterproductive for the training both of thoracic and general surgery residents. Training is prolonged for all residents and the specialty case load experience is diluted for those going into general surgery. Another potential disadvantage is that thoracic surgeons would not have the same latitude in clinical privileges for general surgery operations because they lacked board certification in general surgery. However, it is increasingly difficult to main-

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tain the same standards of care as those who are practicing general surgery full-time. Thus, the medical-legal climate and quality assurance programs make it increasingly difficult for a thoracic surgeon to defend adverse events that occur during the clinical practice that is outside their primary area of clinical specialization. Thus, the value of being "double-boarded" is diminishing each year.

An alternative proposal for restructuring thoracic training is the development of separate training programs and certification for general thoracic surgery and cardiac surgery. Separation of training in general thoracic surgery and cardiac surgery would produce narrowly trained surgeons lacking skills to handle diagnostic and therapeutic problems closely related to their specialty. This will result in a decrement in the quality of thoracic surgical care. Dr Orringer summarizes the case for maintaining unity in his accompanying editorial [2].

Changing the length and mix of thoracic surgical training is only a partial solution. Improvement in general thoracic training will not be possible without dedicated general thoracic surgery faculty. However, there is a shortage of thoracic surgery practitioners in residency programs. This is in part due to the changing character of academic practice. Academic surgical units have become the financial underpinning for hospitals and medical schools rather than centers of teaching and research. Academic advancement is dependent on research productivity. The complexity of contemporary research, requiring advanced training in molecular biology and other basic sciences, adds years to an already lengthy program. The current scarcity of research funding is a serious disincentive.

Is there a solution? The issue is extraordinarily complex and cannot be solved only by the American Board of Thoracic Surgery or the Residency Review Committee. It will require a concerted effort by program directors, department chairpersons, and the thoracic surgery community. Incentives for medical students and residents to enter an academic career in general thoracic surgery are needed. Recruitment of general thoracic surgeons as teachers and role models is needed. The establishment of general thoracic surgery as a separate administrative unit with designated operating time, beds, and research resources will facilitate recruitment. Academic salary scales must be competitive.

Flexibility must be added to the residency. Core training in cardiac and general thoracic for 1.5 to 2 years can be followed with specialized training in thoracic oncology, pediatric cardiac surgery, or other areas of interest. For those interested in an academic career, a minimum 2 years of uninterrupted laboratory research is needed. Program accreditation should be contingent on adequate general thoracic surgical training. Programs that cannot meet the increased requirements can affiliate with specialized centers or can convert to fellowship programs.

Recent data from the Liaison Committee questionnaire show that little change has occurred in the status of general thoracic surgery training over the past 10 years. The problems are clearly defined. It is time to implement effective solutions.

References

1. Peters RM. Should we care? Do we care? What should we do? Ann Thorac Surg 1991;51:807–8.
2. Orringer MB. General thoracic surgery—issues and direction. Ann Thorac Surg 1991;51:814–7.

What Next in Cardiothoracic Training?

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Prompted by Peters' [1] challenge to take a new look at resident education, the foregoing solicited editorials [2–4] represent the first opportunity to review at one time the viewpoints of leaders who have focused on either cardiac surgery or general thoracic surgery, or oncologic surgery. Orringer's [5] comments about a decade of Liaison Committee discussions illustrate that leadership emanating from group deliberations is a slow process.

The common denominators among the viewpoints that have been expressed include agreement that, within thoracic surgery, there are the subspecialties of cardiac surgery for adults, pediatric cardiac surgery, and general thoracic surgery. The representative of each subspecialty argues in favor of more commitment to education, more teachers, and greater concentration of the time framework within which the learning experience takes place. The words *more* and *greater*, at least in part, translate into allocation of resources. The competition for time in the life of our trainees, and resources that derive from our institutions and our practices, is clear. All parties adhere to the unity of cardiothoracic surgery and to the merits of broadly based prerequisite training in general surgery. Nonetheless, there is evidence of competition for time and resources among general surgery, the component parts of cardiothoracic surgery, and thoracic oncology. There is unanimity that the status quo requires revision.

See also page 807.

There are two inseparable goals of thoracic surgery education: to ensure patient welfare by training competent practitioners and to assure perpetuity of excellence through the training of competent teachers. The educators must be so broadly trained as to have the ability to continue to learn and to adapt to ever-expanding knowledge.

As previously stated [6], thoracic surgery should work swiftly at developing new curricular options that consider residents to be postgraduate students. To pay for this necessary luxury, thoracic surgery must convince hospitals and third-party payors that the students render many hours of part-time services that are equal in value to those of independently practicing, fully trained general surgeons. A core curriculum, perhaps entitled "cardiothoracic surgery," should include thoracic oncology and other elective time that will allow trainees to begin focusing on the diseases in which they intend to subspecialize.

It is clearly time to consider the possibility of an abridged general surgery prerequisite that is nonetheless sufficiently substantive to qualify graduates for examination by the American Board of Surgery. A Liaison Committee between general surgery and cardiothoracic surgery should develop curricular segments within each of these specialties in which trainees from the other discipline will be ensured of an experience adequate to meet the needs of the parent specialty.

Only a few training centers can offer truly excellent instruction and experience in all of the specialties of cardiothoracic surgery. Thus, there may be a need for mutually beneficial exchange of trainees from one approved program to another to achieve true excellence in core programs. Training centers approved for core programs should be evaluated as to what supplementary training opportunities they might (or might not) be able to offer.

What would be the net result? There might be fewer trainees nationwide. General surgery training would be shorter and cardiothoracic programs would be longer. There would be a cadre of approved residencies (approximately the same as currently approved programs) with a curriculum that would include a core experience in cardiothoracic surgery. Still within the required period of training, there would be elective time in cardiac surgery for adults, general thoracic surgery, pediatric cardiac surgery, and thoracic oncology. Completion of an approved residency would equip a trainee to be examined by the American Board of Thoracic Surgery. There would be a few centers approved to offer supplementary training in each of the four subspecialties of cardiothoracic surgery. Completion of approved supplementary training would prepare an individual for a subspecialty practice and for an academic position.

To make this proposal a reality would require tremendous energy, sacrifice, and willingness to change on the part of training program directors. We need to make education our priority.

References

1. Peters RM. Should we care? Do we care? What should we do? Ann Thorac Surg 1991;51:807–8.
2. Roth JA, Balch CM. Thoracic surgery training: it is time for a change. Ann Thorac Surg 1991;51:818–9.
3. Grillo HC. Dilemmas in cardiothoracic surgical education. Ann Thorac Surg 1991;51:809–11.
4. Kirklin JW. Training for cardiac surgery in children and adults. Ann Thorac Surg 1991;51:812–3.
5. Orringer MB. General thoracic surgery—issues and direction. Ann Thorac Surg 1991;51:814–7.
6. Benfield JR. The anatomy of peer review. J Thorac Cardiovasc Surg 1991;101:190–5.

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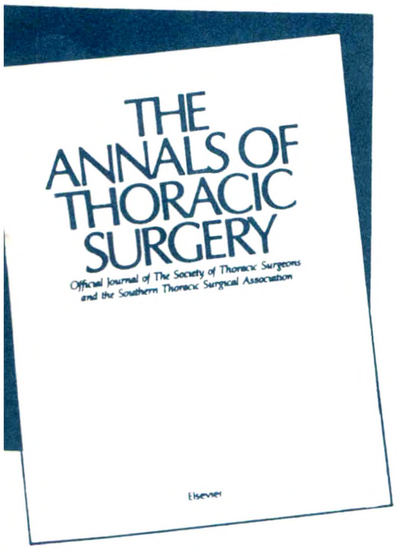
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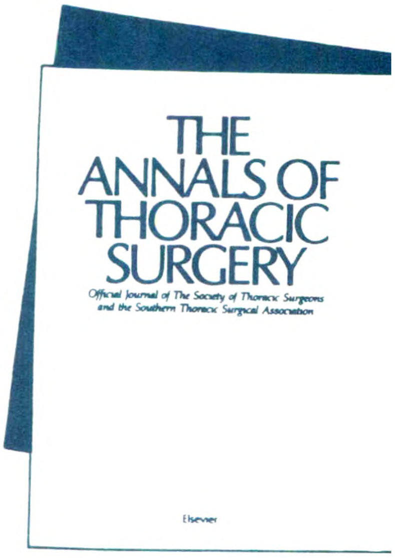
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Traumatic Mitral Valve Rupture in a Child

David McCrory, FRCSI, Brian Craig, MRCP, and Hugh O'Kane, FRCS

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The case of a 6-year-old boy who ruptured his mitral valve after blunt chest trauma and who subsequently had successful mitral valve replacement with a size 25 St. Jude Medical prosthesis is reported. The diagnosis, investigation, and treatment of traumatic valvar rupture are discussed.

(Ann Thorac Surg 1991;51:821–2)

A 6-year-old boy was struck by a car on the left side of his body on August 24, 1987. On admission to the local hospital he was noted to have sustained a fractured right radius and ulna, fractured left femur, and abrasions to the left side of his face and chest. His blood pressure was 90/50 mm Hg and his pulse rate was regular at 170 beats/min; two heart sounds were heard and no murmurs were detected. Respiratory examination was unremarkable. Chest roentgenography was normal and electrocardiography was not carried out. He was taken to the operating theater and the fractures were stabilized.

Overnight his blood pressure remained around 90/50 mm Hg. His urinary output was only 30 mL over a 4-hour period. His intravenous fluids were then increased and in total he was given 540 mL of packed cells and 900 mL of a 4% dextrose/0.18% saline mixture over a 12-hour period. Increasing respiratory difficulties developed despite treatment with diuretics and venesection of 200 mL of blood. His arterial oxygen tension was 4.8 kPa (normal range, 12.0 to 14.7 kPa) on room air and 5.8 kPa with 40% oxygen by face mask. An endotracheal tube was inserted and ventilation commenced. He was transferred to the Royal Belfast Hospital For Sick Children 24 hours after injury. On admission he was noted for the first time to have a harsh systolic murmur maximal at the apex. Chest roentgenography showed increased pulmonary vascularity and an enlarged left ventricle; ST depression in leads 2, V_4, V_5, and V_6 was noted on electrocardiography. Serum cardioselective enzyme levels (creatine kinase-MB) were elevated at 169 U/L (normal range, 0 to 35 U/L). Echocardiography confirmed the presence of marked mitral regurgitation with ruptured papillary muscle and good left ventricular function.

He was treated conservatively with digoxin and diuretic therapy and was gradually weaned from assisted ventilation. His condition remained stable while he was immobilized and the fractures healed well. As he began mobilization he was dyspneic even on mild exertion despite diuretic, digoxin, and vasodilator therapy. In light of this a cardiac operation was performed 12 weeks after injury. At operation the anterolateral papillary muscle was found to be ruptured but was obviously necrotic and beyond repair. The valve was excised and replaced with a size 25 St. Jude Medical prosthesis. He was discharged home 14 days after operation on a regimen of furosemide, spironolactone, digoxin, and warfarin. At his last review in March 1990 he was in excellent health. Diuretics were no longer required and he continues to receive digoxin and warfarin.

Comment

Rupture of the heart valves after blunt chest trauma is rare. Isolated valvar rupture most commonly affects the aortic valve, followed by the mitral valve and least commonly the tricuspid valve [1, 2]. Mitral valve rupture may affect various parts of the valvar mechanism. Rupture occurs when trauma takes place at the beginning of systole. This is when intracardiac pressures are at their highest and the added pressure of chest compression is enough to rupture the valvar apparatus. Papillary muscle rupture is the most usual injury, as was seen in this case [3]. Less commonly the chordae tendineae rupture, and least common of all is laceration to the valve cusp [3]. Blunt trauma may result in instant papillary muscle rupture if compression forces are large enough. However, as each papillary muscle is supplied by a long central artery, ischemia may ensue with later infarction and rupture if this artery is damaged [4].

Mitral valve rupture should be suspected after trauma if a systolic murmur is heard in a patient with no previous cardiac history. The blood pressure is often low and the patient may become dyspneic and have pulmonary edema. Signs and symptoms may be misinterpreted. Low blood pressure may be attributed to hypovolemia secondary to other injuries. Dyspnea may be wrongly ascribed to lung contusion, aspiration pneumonia, fat embolism, adult respiratory distress syndrome, or over-hydration. The initial management in this case emphasizes these points. The low blood pressure was originally thought to be due to hypovolemia, and hence he was over-hydrated. This ultimately exacerbated any pulmonary symptoms that were going to develop because of his mitral regurgitation. The respiratory difficulties were then solely attributed to over-hydration and diuretics were given and venesection performed.

Diagnosis is aided by chest roentgenography, which often shows pulmonary edema. The left atrium is small, which is typical of recent onset rather than long-standing

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mitral regurgitation. A low oxygen tension is found on arterial blood gas analysis. An electrocardiogram should be carried out in all cases of chest trauma. It may show ischemic changes, as was the case with this patient after transfer to the children's hospital. If an electrocardiogram had been carried out earlier it may have alerted the staff in the original hospital to the possibility of cardiac trauma, thereby preventing the initial mismanagement of this patient's fluid balance. Even if the electrocardiogram is normal it will act as an accurate base line against which to judge any subsequent recording. Echocardiography is diagnostic in mitral valve rupture. It can identify rupture of the chordae or papillary muscles, valvar prolapse, or flail cusps [5, 6]. It is reliable, easily performed, and a noninvasive diagnostic tool. In this case it was relied on completely and cardiac catheterization was not deemed necessary.

With mitral valve rupture early diagnosis and treatment is essential as rapid deterioration may occur. There have been cases reported of papillary muscle fibrosis after injury thus allowing an adequate degree of mitral valve competence to remain [4]. It was decided for this reason to attempt to treat this child conservatively. Conservative management was possible while he was immobilized to allow his fractures to heal and he remained completely asymptomatic. This accounted for the bulk of the 12-week period before operation. Only when mobilization was commenced did he suffer persistent dyspnea, and mitral valve replacement was then performed. Mitral valve reconstruction was not possible because of the marked necrosis in the papillary muscle.

In children of this age we recommend that conservative management should be the first line of treatment, clinical status permitting. When operation is undertaken repair of the valvar apparatus should be attempted where possible and prosthetic replacement used only as a last resort. Successful repair avoids the obvious hazards of prosthetic replacement such as thrombosis, long-term anticoagulation, and endocarditis. Repair is particularly important in children as the valve ring may only allow the insertion of a small prosthesis, which may not be functionally large enough to cope with later growth.

References

1. Rumisek JD, Robinowitz M, Virmani R, Barry MJ, Steudel T. Bioprosthetic heart valve rupture associated with trauma. J Trauma 1986;26:276–9.
2. Flejou Y, Roland E, Ecoiffier J. The place of angiography in the evaluation of traumatic injuries to the heart and coronary arteries. Cardiovasc Radiol 1979;2:47–50.
3. Scorretti C. Traumatic rupture of the anterior papillary muscle. Z Rechtsmed 1983;91:153–7.
4. Devineni R, McKenzie FN. Acute mitral insufficiency resulting from blunt chest trauma. J Thorac Cardiovasc Surg 1983;85:797–8.
5. Miller SW, Deluca SA. Ruptured chordae tendineae. Am Fam Physician 1984;30:125–6.
6. Mintz GS, Kotler MN, Segal BL, Parry WR. Two-dimensional echocardiographic recognition of ruptured chordae tendineae. Circulation 1978;57:244–50.

Preoperative Erythropoietin in Jehovah's Witnesses Who Require Cardiac Procedures

Vincent A. Gaudiani, MD, and H. Duncan W. Mason, MD

Cardiovascular Surgery, Sequoia Hospital, Redwood City, California

This report details the preoperative use of recombinant human erythropoietin in 2 Jehovah's Witnesses who required elective cardiac operations.

(Ann Thorac Surg 1991;51:823–4)

Jehovah's Witnesses create a special problem for the cardiac surgeon by their refusal to accept stored blood, even autologous units. We recently employed recombinant human erythropoietin (Epogen; Amgen Corporation, Thousand Oaks, CA) in 2 Jehovah's Witnesses. After informed consent was obtained and the blood pressure measured, laboratory measurements including a complete blood cell count, reticulocyte count, and measurement of serum iron and iron binding capacity were made. Both patients were treated with ferrous gluconate, 300 mg three times daily, and folic acid, 1 mg daily. Epogen was administered at a dose of 100 μg/kg subcutaneously three times a week for 3 weeks. Twice a week microstick hemograms were obtained and blood pressure was checked.

For editorial comment, see page 703.

Case Reports

Patient 1

A 40-year-old normotensive woman with a 20-year history of mitral valve prolapse was seen with progressive congestive heart failure. Echocardiographic examination demonstrated 4+ mitral regurgitation with well preserved left ventricular function. Body weight was 62 kg and hematocrit 0.34 despite several weeks of iron and folate therapy. She was believed to be at increased risk for operative repair and was therefore treated with erythropoietin as described in the preceding section. During therapy her reticulocyte count increased from 5×10^{-3} to 40×10^{-3} and her hematocrit to 0.45. At operation a unit of blood was withdrawn but left in continuity with the intravenous line as per her request. She did agree to the intraoperative use of the Cell-Saver. During operation using a conventional bubble oxygenator and 1,300 mL of crystalloid prime, her hematocrit decreased to 0.30. The valve was a typical myxomatous structure with torn posterior chordae. A quadrilateral resection was performed, secured with a Carpentier ring. Total time on cardiopulmonary bypass was 73 minutes with a cross-clamp time of 43 minutes. The previously removed unit of blood was reinfused at the end of the procedure. The first hematocrit after return to the intensive care unit was 0.40, and it never decreased to less than 0.38 during a 6-day postoperative hospitalization. No further erythropoietin was used. An echocardiogram 6 months later revealed no mitral regurgitation, and the patient's hematocrit was once again 0.34.

Patient 2

A 63-year-old, 87-kg, diabetic woman with a history of hypertension (blood pressure, 170/90 mm Hg) and several previous myocardial infarctions was seen with intermittent congestive heart failure, multivessel coronary artery disease, and an ejection fraction of 0.25. Her hematocrit, despite three months of iron and folate therapy, was 0.36 associated with a reticulocyte count of 18×10^{-3}. After 3 weeks on the erythropoietin protocol, her reticulocyte count had increased to 45×10^{-3} and her hematocrit to 0.41. Her hypertension remained easy to control. Once again a unit of blood was withdrawn before initiation of cardiopulmonary bypass but remained in continuity with the intravenous line. Her coronary arteries were diffusely diseased and difficult to manage. A cross-clamp time of 99 minutes and a total bypass time of 144 minutes were required to construct four vein grafts and perform a left anterior descending endarterectomy. Her hematocrit decreased to 0.28 during cardiopulmonary bypass, but increased to 0.34 after decannulation and reinfusion of the stored unit. The postoperative period was complicated by an episode of ventricular tachycardia on the third postoperative day requiring cardioversion. Her hematocrit, which decreased to a minimum of 0.27 on the second postoperative day, gradually increased to 0.34 with resumption of her preoperative regimen of erythropoietin, iron, and folic acid. Otherwise her hospitalization was uneventful, allowing for discharge on the 14th postoperative day. She currently experiences mild congestive heart failure requiring therapy with furosemide, digoxin, and captopril.

Comment

Preoperative use of recombinant human erythropoietin adds to the safety of a cardiac procedure by raising the

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hematocrit and preparing the bone marrow for high-volume red cell production. By blunting the usual decline in hematocrit, recovery is accelerated and care simplified by improvement in appetite and exercise tolerance as well as improvement in central nervous system and other organ function [1–3]. Although we did not measure preoperative erythropoietin levels, we can assume, based on the reticulocyte response, that the drug was effective.

Earlier studies have demonstrated the relative safety of this agent in dialysis-dependent renal failure [4, 5]. Although complications including uncontrolled hypertension and seizures have been reported [5, 6], these risks can be minimized by advising against driving and by performing twice weekly hemogram and blood pressure checks. All patients under treatment exhibit a loss of iron stores, and iron deficiency results in a suboptimal response to erythropoietin; hence the need for replacement therapy [1, 7]. Immunogenicity and drug interactions have not been reported [5–7].

A vial of erythropoietin contains 2.5 mg of human albumin and complicates the issue of informed consent. We wonder if it adds to informed consent or merely burdens the patient to discuss such fine points in detail. Ultimately the management of such ethical issues is a matter of personal practice style, but in general we confine our discussions to the administration of whole blood, its formed elements, or any constituent that may transmit disease or generate an immunological response. Should the patient wish more detail, we oblige.

In conclusion, we believe that human recombinant erythropoietin has a place in the management of appropriately selected and informed Jehovah's Witness patients undergoing elective cardiac surgical procedures.

References

1. Mohini R. Clinical efficacy of recombinant human erythropoietin in hemodialysis patients. Semin Nephrol 1989;9(Suppl 1):10–21.
2. Eschbach JW, Kelly MR, Haley NR, Abels RI, Adamson JW. Treatment of the anemia of progressive renal failure with recombinant human erythropoietin. N England J Med 1989; 321:158–63.
3. Lundin AP. Quality of life: subjective and objective improvements with recombinant human erythropoietin therapy. Semin Nephrol 1989;9(Suppl 1):22–9.
4. Goodnough LT, Rudnick S, Price TH, et al. Increased preoperative collection of autologous blood with recombinant human erythropoietin therapy. N Engl J Med 1989;321:1163–8.
5. Eschbach JW, Egric JC, Downing MR, Browne JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. N Engl J Med 1987;316: 73–8.
6. Casati S, Passerini P, Campasi M, et al. Benefits and risks of protracted treatment with human recombinant erythropoietin in patients having hemodialysis. Br Med J 1987;295:1017–20.
7. Flaharty KK, Grimm AM, Vlasses PH. Epoetin: human recombinant erythropoietin. Clin Pharm 1989;8:769–82.

REVIEW OF RECENT BOOKS

Current Practice of Surgical Stapling

Edited by Mark M. Ravitch, MD, Felicien M. Steichen, MD, and Roger Welter, MD
Philadelphia, Lea and Febiger, 1991
324 pp, illustrated, $79.50

Reviewed by Harold V. Gaskill III, MD

This book is composed of 51 chapters prepared by select participants at the Second International Symposium and First European Congress on Stapling in Surgery held in Luxembourg in 1988. The subject of surgical stapling is divided into 10 parts. Part 1, entitled "History and Principles of Stapling in Surgery," presents Dr Ravitch's historical perspective and personal viewpoint beginning with his trip to Kiev in 1958. Although this story is by now well known to many, it is presented concisely and with a number of historically significant photographs. Dr Steichen then continues with a review of the evolution of mechanical sutures and mechanical suturing machines. Again, there is generous use of diagrams and photographs of these early designs. Also included in part 1 is an excellent chapter on "The Teaching and Learning of Stapling." Fundamental principles such as the proper placement of the pursestring suture and careful inspection of tissue donuts are presented in 4 concise pages.

Although the book focuses primarily on surgical stapling, the use of such related techniques as compression anastomosis and biological glue are also discussed. The special topics of stapled wound healing and healing of irradiated tissue, as well as morbidity and mortality associated with stapling procedures, are also addressed.

The remainder of the book is organized by organ systems with separate parts covering the lungs, esophagus, stomach, and colorectum. The use of stapling procedures at the esophagogastric or esophagojejunal junction is also addressed separately. Each of these parts comprises between four and eight articles focusing on some particular aspect of the region. Thus, the section on stapling and pulmonary surgery includes not only a paper entitled, "The Use of Stapling Devices in Pulmonary Surgery," but also sections covering more focused topics such as "The Value of Staplers in Operations for Spontaneous Pneumothorax" and "Technique of Tissue Saving Pulmonary Resections Using the Linear GIA Stapling Device." The quality of the articles is uniformly high and generous use of photographs and drawings continues throughout the text. Despite its small size, this text should not be regarded as simply a primer on surgical stapling, nor should it be regarded as the ideal text for a surgical resident with no prior exposure to surgical stapling. Rather, it should be viewed as a select collection of articles generated by pioneers, past and present, of the field.

After Dr Mark Ravitch's lifelong interest in the field of mechanical wound closure, his death during the preparation of this text has given it a special significance. This is touched on briefly by Dr Steichen in the forward. It is likely that anyone who shares even a fraction of Dr Ravitch's enthusiasm for the field would be pleased to add a copy of this book to his or her personal library.

San Antonio, Texas

Use of Human Recombinant Erythropoietin to Correct Severe Preoperative Anemia

David A. Fullerton, MD, David N. Campbell, MD, and Glenn J. R. Whitman, MD

Department of Surgery, University of Colorado Health Sciences Center, Denver, Colorado

The risks of homologous blood transfusion are well known. Herein, we describe the successful preoperative use of human recombinant erythropoietin to correct severe anemia in a patient refusing transfusion. This case report emphasizes the important perioperative role human recombinant erythropoietin may play in the future.

(Ann Thorac Surg 1991;51:825–6)

Cardiovascular surgical procedures are frequently associated with substantial blood loss. Autologous blood donation may diminish the need for homologous blood transfusion [1], but it is not always feasible. Despite efforts to minimize intraoperative blood loss and the use of perioperative blood salvage, it is frequently impossible to safely perform major procedures with homologous transfusion.

In the primate model, human recombinant erythropoietin has demonstrated remarkable potential to accelerate perioperative erythropoiesis [2–4]. Herein we report the successful use of preoperative human recombinant erythropoietin to correct severe preoperative anemia in a patient who refused blood transfusion on religious grounds.

For editorial comment, see page 703.

A 54-year-old woman had intermittent chest pain in the anterolateral left chest. Seventeen years previously she had had tube graft bypass of a thoracic aortic coarctation. Her medical history was also significant for chronic renal insufficiency, and she had a creatinine level of 220 μmol/L (2.5 mg/dL) and anemia (hematocrit, 0.30) of unknown cause.

On this admission, her chest roentgenogram revealed a large left mediastinal mass. Cardiac catheterization revealed normal coronary arteries. However, she had an 8-cm pseudoaneurysm of the thoracic aortic tube graft. After catheterization she hemorrhaged from her right femoral artery, culminating in a decrease in her hematocrit to 0.22. Surgical correction of the pseudoaneurysm was recommended to the patient, to which she agreed. However, for religious reasons, she adamantly refused to accept blood transfusion. She did, however, give informed consent to the use of human recombinant erythropoietin.

The patient was therefore treated with human recombinant erythropoietin, 100 units/kg, given intravenously three times weekly. This dose was lower than but consistent with the dose used in patients with renal failure [5]. She received this therapy in addition to oral iron sulfate and folate supplementation on an outpatient basis. Before administration of human recombinant erythropoietin, her reticulocyte index was 5×10^{-3}. After 2 weeks, her reticulocyte index was 3.0% and her hematocrit was 0.31. She remained clinically stable for 19 days, during which time her hematocrit increased to 0.39. On the 20th day the patient experienced acute left chest pain and was readmitted with impending rupture of the thoracic pseudoaneurysm. The patient was taken urgently to the operating room for repair.

At operation, a pseudoaneurysm of the proximal suture line was found. The original tube graft was replaced with a new 22-mm bypass graft. Estimated intraoperative blood loss was 750 mL, which was reinfused using intraoperative autotransfusion. The patient's hematocrit at the end of the procedure was 0.34.

Postoperatively the patient did well and was again given oral iron supplements. At discharge her hematocrit was 0.26. At 6 months, she had reestablished her long-term hematocrit of 0.30 (Fig 1).

Comment

The risks of homologous transfusion primarily entail the risks of transfusion reaction (hemolytic or leukoglutinin) and disease transmission. Hepatitis remains the most common disease transmitted, at a rate of 4% to 6% per unit, with the risk of hepatitis B approximately 0.4% per unit [6, 7]. Chronic active hepatitis develops in approximately one third of patients contracting hepatitis [6]. Other viruses transmissible by transfusion include cytomegalovirus, Epstein-Barr virus, parvovirus, and human T-cell lymphotropic viruses [7].

The risk of transmission of human immunodeficiency virus is estimated to be between 1:40,000 and 1:100,000 [7]. However, several years may elapse before patients with documented human immunodeficiency virus infection become seropositive [8]. The obvious implication is that available screening techniques may fail to identify blood capable of transmitting human immunodeficiency virus.

These risks have strongly motivated efforts to minimize or avoid homologous transfusion. Such efforts include autotransfusion, hemodilution, and autologous transfusion. In most programs of preoperative autologous dona-

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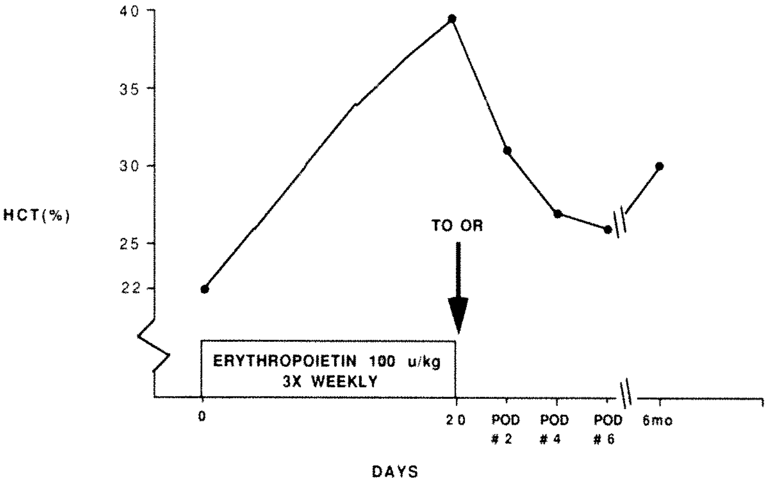

Fig 1. Improvement in preoperative hematocrit (HCT) with erythropoietin therapy. (OR = operating room; POD = postoperative day.)

tion, patients may donate one unit per week provided their hemoglobin level is at least 110 g/L [1]. Thus, 4 to 6 weeks of preoperative donation may be required for major procedures. This time frame may prove excessive when operation may not be deferred such as in emergent situations or major oncologic resections.

Recombinant human erythropoietin may have a major impact on the problems of perioperative anemia. It corrects the anemia of renal insufficiency, eliminating the need for transfusion [5]. It has been remarkably effective in the baboon model to correct perioperative anemia and to shorten the time required to autodonate six units of blood from 6 weeks to 2 weeks [2–4]. The implications for human autologous blood donations are obvious.

The current case report illustrates the value of recombinant human erythropoietin in the clinical perioperative situation. Within 3 weeks, our patient's hematocrit increased from 0.22 to 0.39. This augmentation provided a margin of safety that allowed the performance of a major surgical procedure without homologous transfusion. This case confirms the clinical applicability of the experimental perioperative primate data and emphasizes the important perioperative role human recombinant erythropoietin may play in the future.

References

1. Council on Scientific Affairs. Autologous transfusion. JAMA 1986;256:2378–80.
2. Levine EA, Gould SA, Rosen AL, et al. Perioperative recombinant human erythropoietin. Surgery 1989;106:432–8.
3. Levine EA, Rosen AL, Gould SA, et al. Recombinant human erythropoietin and autologous blood donation. Surgery 1988; 104:365–9.
4. Levine EA, Rosen AL, Lakshman RS, et al. Treatment of acute postoperative anemia with recombinant human erythropoietin. J Trauma 1989;29:1134–9.
5. Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. N Engl J Med 1987;316: 73–8.
6. Greenburg GA. Indications for transfusion. In: Wilmore DW, ed. Care of the surgical patient. New York: Scientific American, 1989:1–19
7. Office of Medical Application of Research, National Institutes of Health. Perioperative red cell transfusion. JAMA 1988;260: 2700–3.
8. Imagawa DT, Moon HL, Wolinsky SM, et al. Human immunodeficiency virus type I infection in homosexual men who remain seronegative for prolonged periods. N Engl J Med 1989;320:1458–62.

Infected Intravenous Port Device Causing Tricuspid Valve Regurgitation

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Sepsis and tricuspid valve regurgitation developed in a 29-year-old man with Crohn's disease after implantation of an intravenous port device for parenteral nutrition. A thrombus, caused by *Staphylococcus epidermidis*, had grown along the catheter and prolapsed through the valve without affecting it. Complete removal in an open heart procedure led to quick recovery.

(Ann Thorac Surg 1991;51:827–8)

Intravenous port devices are implanted for a variety of indications. Although thought to be safe catheters for long-term use, severe complications may occur, even necessitating relief by open heart operation.

A 29-year-old man with Crohn's disease underwent drainage of a retroperitoneal abscess. To enable prolonged total parenteral nutrition for a spell of several months at home, an intravenous port device was implanted through the left cephalic vein. Eighteen days after this operation septic temperatures up to 38.5°C developed, persisting despite intravenous antibiotic treatment. Multiple small cutaneous abscesses rapidly developed. Blood cultures detected *Staphylococcus epidermidis*, an organism that had not been found in swabs from the retroperitoneal abscess. Antibiotic treatment was changed according to the antibiogram.

Conventional and transesophageal echocardiography and Doppler sonography revealed marked thickening of the port catheter from the superior vena cava into the right atrium. A vegetation originating from this thickened catheter was seen prolapsing through the tricuspid valve causing regurgitation. It was not adherent to a cardiac structure. The tricuspid valve itself looked unaffected.

The patient was transferred to have the port system explanted and the tricuspid valve revised. He had a central venous line placed through his right femoral vein to stay away from the potentially infected right atrium. Immediately before the incision, one dose of the last antibiotic regimen (vancomycin, 500 mg, and piperacillin, 4 g) was given.

The operation was performed through a sternotomy. Simultaneously the port device was dissected free. After pericardiotomy, both venae cavae were dissected, then aorta and inferior vena cava were cannulated. Cardiopulmonary bypass was started with the patient cooled to moderate hypothermia of 30°C. After induction of ventricular fibrillation, aorta and pulmonary artery were clamped, the latter to prevent embolization of septic material. One liter of cold crystalline cardioplegic solution was given through the aortic root.

After right atriotomy the venous backflow through the superior vena cava was controlled by suction. A large, pink, thrombuslike vegetation was seen completely enwrapping the catheter of the port device and prolapsing through the tricuspid valve. The tricuspid valve itself looked perfectly normal without any sign of infection. The thrombus was then extracted through the atriotomy while the port catheter was carefully retracted out of the cephalic vein. The vegetation was 10 cm in length and about 1 cm in diameter (Fig 1). After closure of the superior vena cava, a second venous cannula was inserted and rewarming started. After closure of the atriotomy and deairing, pulmonary artery and aorta were released. Total aortic cross-clamping time was 12 minutes. The heart started beating in sinus rhythm spontaneously. After decannulation (total bypass time, 23 minutes) the chest was closed with steel wires, and the skin was closed with single nonabsorbable stitches. The wound at the port implantation site was repeatedly irrigated with iodine and drained.

Postoperatively, the antibiotic regimen was continued. Cardiopulmonary recovery was uneventful. Both wounds healed primarily. The antibiotic regimen was continued for 4 weeks and there was no recurrence of septic events. Echocardiography showed a fully competent tricuspid valve without morphological changes 4 weeks postoperatively.

Comment

Sustained venous access is needed for the treatment of a variety of diseases. Because of numerous complications associated with the long-term use of catheters of the Broviac or Hickman type, which exit through the skin, fully implantable devices were developed. Worldwide experience has been gained since their first clinical use was reported in 1982 [1]. Port devices are used for the infusion of chemotherapeutic agents, antibiotics, blood products, and parenteral nutrition in chronically ill patients, usually with compromised immune reactions.

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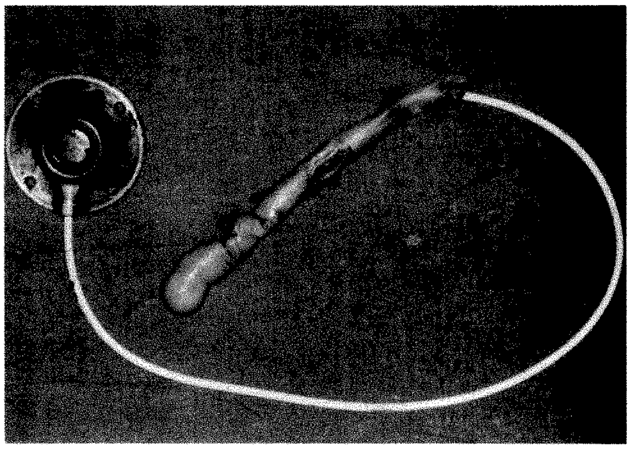

Fig 1. Septic thrombus and port device after removal. (Length of thrombus, 10 cm; diameter, 1 cm.)

With time, the same problems emerged as with the old-fashioned catheters, that is, mainly thrombosis and infection [2, 3]. One study even revealed comparable incidences of infectious complications for both catheter types [4]. Nevertheless, intravenous port devices have become accepted by physicians and patients to be the most comfortable way of chronic venous access, because catheter-related morbidity and mortality are still very low.

Correct positioning of the catheter tip in the superior vena cava makes the right side of the heart prone to catheter-induced lesions. An incidence of mural thrombi caused by central venous catheters of up to 29% has been found in a postmortem study [5]. Embolization and secondary infection of thrombi are common further complications.

In patients with long-standing central venous catheters, skin and mucous membrane commensal gram-positive organisms have been found to be the most common group of pathogens causing bacteremia [4, 6, 7]. Especially coagulase-negative staphylococci such as *S epidermidis* have the ability to become adherent to polymer surfaces. These organisms produce a mucuslike substance in which they become enwrapped. This in turn enhances their adherence to surfaces and protects them from direct contact with antibiotics. Opsonization by granulocytes is also hindered [8]. These special properties explain how even an extremely large septic thrombus, such as encountered in our case, can grow despite antibiotic treatment without producing more severe systemic reactions.

Although successful treatment of infected central venous catheters by antibacterial therapy has been described [2–4, 7], the necessity of surgical removal of the implanted device in our case is obvious. Such an involvement of the right side of the heart makes an open heart procedure mandatory to prevent septic embolization into the lungs, to ascertain complete removal and to evaluate the endocardium and the tricuspid valve.

This case illustrates that strange and severe complications may develop in patients bearing intravenous port devices or, in fact, all kinds of central venous catheters. Even discrete signs of sepsis must make the physician suspicious of catheter infection. Echocardiography, especially transesophageal, is a valuable tool in detecting vegetations along the device. Surgical removal is indicated, if necessary in an open heart procedure.

References

1. Niederhuber JE, Ensminger WD, Gyves JW, Liepman M, Doan K, Cozzi E. Totally implanted venous and arterial access system to replace external catheters in cancer treatment. Surgery 1982;92:706–11.
2. Bothe A, Piccione W, Ambrosino JJ, Benotti PN, Lokich JJ. Implantable central venous access system. Am J Surg 1984; 147:565–9.
3. Brothers TE, Von Moll LK, Niederhuber JE, Roberts JA, Walker-Andrews S, Ensminger WD. Experience with subcutaneous infusion ports in three hundred patients. Surg Gynecol Obstet 1988;166:295–301.
4. Wurzel CL, Halom K, Feldman JG, Rubin LG. Infection rates of Broviac-Hickman catheters and implantable venous devices. Am J Dis Child 1988;142:536–40.
5. Ducatman BS, McMichan JC, Edwards WD. Catheter-induced lesions of the right side of the heart. A one-year prospective study of 141 autopsies. JAMA 1985;253:791–5.
6. Lazarus HM, Lowder JN, Herzig RH. Occlusion and infection in Broviac catheters during intensive cancer therapy. Cancer 1983;52:2342–8.
7. Pessa ME, Howard RJ. Complications of Hickman-Broviac catheters. Surg Gynecol Obstet 1985;161:257–60.
8. Peters G. Plastikinfektionen durch Staphylokokken. Dtsch Aerztebl 1988;85:B-234–9.

An Unusual Problem During Surgical Removal of a Broken Guidewire

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At operation, it proved impossible using traction alone to remove an angioplasty guidewire that was lodged in an intermediate artery. The problem was solved by passing a Teflon catheter over the wire, thus protecting the left main coronary artery while freeing the entrapped distal end of the guidewire.

(Ann Thorac Surg 1991;51:829–30)

Retained broken guidewires or broken balloon catheters are rare complications of angioplasty procedures, with an incidence estimated at 0.1% to 0.2% [1, 2]. In most cases described in the literature, the foreign material could be removed using percutaneous techniques [1, 3]. In 6 other reported cases, the retained guidewire segments or broken balloon catheters were removed easily at operation through an arteriotomy at the site of an epicardial hematoma [2, 4–8]. Recently, however, we had a patient in whom the distal end of a broken guidewire was lodged in an intermediate branch and in whom we encountered problems during surgical removal.

A 69-year-old man with triple-vessel coronary artery disease underwent a second percutaneous balloon angioplasty of a large intermediate branch that had recently become occluded. During manipulations to cross the stenosis and steer the guidewire into the distal vessel, the wire became lodged in the occluded vessel. On manual traction, it then fractured somewhere in the descending aorta, leaving a fragment attached to the coronary artery. An attempt to remove the guidewire using the snare loop technique failed [3]. During all of this, the patient did not have any chest pain. Emergency operation was then performed to remove the wire and to revascularize the heart.

The heart was normal on inspection. After initiation of extracorporeal circulation, cardiac arrest was induced using topical cooling and aortic root cardioplegia (St. Thomas' Hospital solution). Efforts to catch the guidewire with a hook inserted through the site of puncture of the cardioplegia needle in the ascending aorta were unsuccessful. Coronary artery bypass grafting was performed, and after completion of the distal anastomoses, the ascending aorta was opened by transverse aortotomy. The guidewire was removed easily from the distal part of the aorta, but while traction was applied on the wire to remove it from the left coronary artery, it uncoiled without becoming dislodged. The remnant of the guidewire was transformed into a razor-sharp wire (diameter, 0.08 mm), raising the potential danger that applying more traction would cause the wire to cut through the left main coronary artery. In an effort to reach and free the wire from the other side, the intermediate branch was opened proximal to the anastomosis and the incision was extended proximally without compromising the left main coronary artery. Atheromatous debris was removed but the guidewire was not seen.

Finally, we succeeded in removing the guidewire through the aortotomy by passing a 20-gauge soft Teflon Quick-Cath (Baxter Health Care Ltd, Castlebar, Ireland) catheter, normally used for intravenous infusion, over the guidewire (Figs 1, 2). Inspection of the fragment showed that it had been removed completely. No further problems were encountered. Serial electrocardiograms and enzyme changes demonstrated that the patient had suffered a myocardial infarction in the inferoposterior wall, but despite this, the patient made an uneventful recovery.

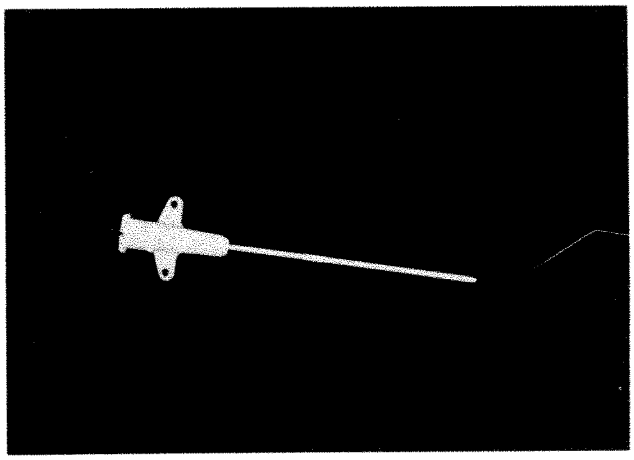

Fig 1. A Quick-Cath Teflon catheter passed over a retained guidewire could prevent injury to the left main coronary artery, while at its tip the wire was uncoiled.

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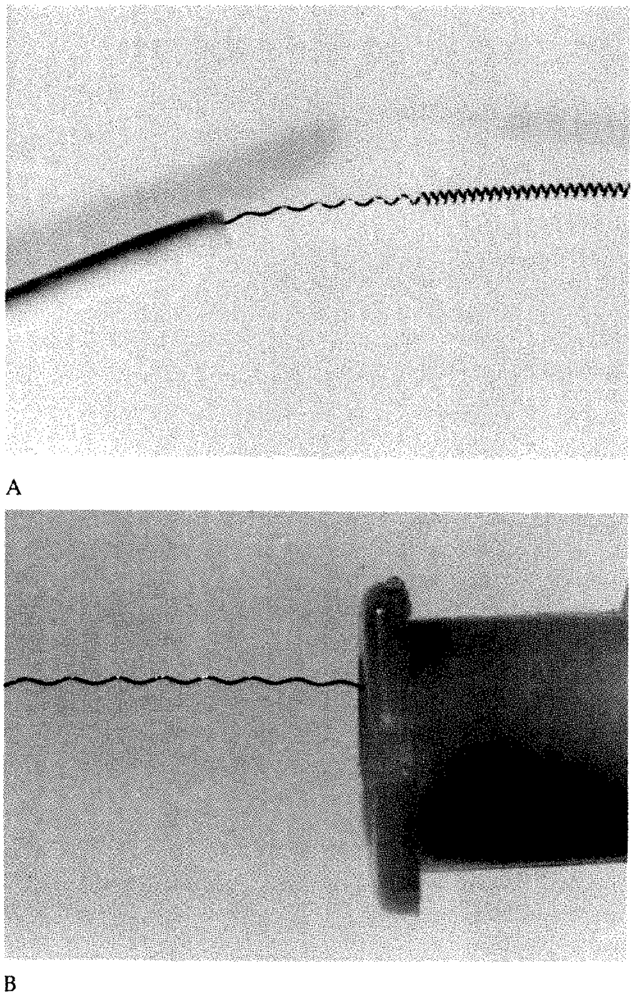

Fig 2. (A) View of the catheter showing the uncoiling of the guidewire. (B) View of the proximal end of the catheter, showing the uncoiled guidewire, which had become razor-sharp (diameter, 0.08 mm). The Quick-Cath protected the inner side of the coronary artery while the guide wire was uncoiled and was removed.

Comment

Several authors [2, 4–8] have reported on the surgical removal of retained percutaneous angioplasty material, and in these reported cases, the retained fragments could be removed easily. Our experience now suggests that the surgical removal of fractured wires is not always straightforward and it may be associated with risks. The reported solution of the problem may be of help to others who have to deal with this complication of modern interventional cardiology. In the future, we suggest that before an entrapped and uncoiled guide wire fractures, an attempt should be made to free the distal part by applying the described technique percutaneously, in which a 3F perfusion catheter is pushed over the stretched guidewire.

References

1. Hartzler GO, Rutherford BD, McConahay DR. Retained percutaneous transluminal coronary angioplasty equipment components and their management. Am J Cardiol 1987;60:1260–4.
2. Van den Brand M, de Feyter P, Serruys PW, Zijlstra F, Bos E. Fracture of a balloon on a wire device during coronary angioplasty. Cathet Cardiovasc Diagn 1989;16:253–7.
3. Watson LE. Snare loop technique for removal of broken steerable PTCA wire. Cathet Cardiovasc Diagn 1987;13:44–7.
4. Proctor MS, Koch LV. Surgical removal of guidewire fragment following transluminal coronary angioplasty. Ann Thorac Surg 1988;45:678–9.
5. Seifert PE, Auer JE. Removal of guidewire fragment [letter]. Ann Thorac Surg 1989;47:638.
6. Khonsari S, Livermore J, Mahrer P, Magnusson P. Fracture and dislodgement of floppy guidewire during percutaneous transluminal coronary angioplasty. Am J Cardiol 1986;58: 855–6.
7. Ghosh PK, Alber G, Schistek R, Unger F. Rupture of guide wire during percutaneous transluminal coronary angioplasty: mechanics and management. J Thorac Cardiovasc Surg 1989; 97:467–9.
8. Döring V, Hamm Ch. Delayed surgical removal of a guidewire fragment following coronary angioplasty. Thorac Cardiovasc Surg 1990;38:36–7.

False Aneurysm of the Right Internal Mammary Artery

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False aneurysm of the internal mammary artery is an uncommon complication of median sternotomy. Clinical and radiological findings of 2 such cases are presented. At operative exploration neither was directly related to the presence of a sternal wire.

(Ann Thorac Surg 1991;51:831–2)

Median sternotomy is a safe and reliable approach to the heart that provides good access and usually secure closure. However, instability with occasional dehiscence is a serious complication, and in some units it has become the practice to place wires around the sternum rather than through it to produce a stronger closure [1]. The anxiety is that inadvertent puncture of the internal mammary artery (IMA) might produce troublesome bleeding, but this is in fact extremely rare. We have encountered another complication, false aneurysm of the IMA, at two different hospitals.

Case Reports

Patient 1

A 68-year-old woman underwent median sternotomy for the excision of a left atrial myxoma under cardiopulmonary bypass. The procedure was well tolerated and uneventful. The initial postoperative course was marked by two episodes of sudden hypotension on the night of the operation; these were easily managed with colloid replacement and small doses of calcium chloride. Her subsequent recovery was uneventful and she was transferred back to her referring hospital for convalescence.

Four weeks after operation, she was noted to have an expansile mass 3 cm in diameter lying in the right fifth intercostal space, alongside the sternal edge. A harsh systolic bruit was audible over the mass.

A contrast-enhanced computed tomographic scan was performed to exclude a false aneurysm arising from the aortic cannulation site. This showed a mass lying anterior to the sternum that was enhanced with contrast medium. A communication with the mediastinum could not be demonstrated (Fig 1).

Within 24 hours of this study it became apparent that the mass had become firm and was no longer expansile. The bruit was no longer audible. Ultrasound showed a mixture of cystic and solid components with a pulsatile cavity communicating with a deeper vessel.

A diagnosis of false aneurysm of the right IMA had been established and the patient underwent an aortogram and selective injection of the IMA with a view to embolization. However, at catheterization the artery appeared normal and it was not possible to demonstrate a false aneurysm.

Operative exploration of the mass showed a false aneurysm 4 cm in diameter arising from a perforating branch of the right IMA in the fifth intercostal space. A wire was not present in that space. The aneurysm was excised, the IMA being ligated both proximal and distal to the aneurysm.

Patient 2

A 69-year-old man underwent median sternotomy for aortic valve replacement. The procedure was uneventful as was his postoperative recovery. He was seen again 4 weeks after his operation, pale and unwell, with a hot, pulsatile, swelling 2 cm in diameter along the right sternal edge. A diagnosis of mycotic false aneurysm was made, and it was presumed to be related to the aortic incision or aortic cannulation site.

A computed tomographic scan, which had already been ordered by his cardiologist (Fig 2), was unequivocally reported as confirming aortic false aneurysm. With hindsight, the diagnosis might have been questioned because a communication was not seen, and the early filling of the aneurysm with contrast medium was accepted as evidence of arterial communication. Aortography was not requested. The chest was reopened through the previous median sternotomy after femoral arterial cannulation. The false aneurysm was found to be quite separate from the aorta, which was intact.

A wire was not present in the intercostal space. After surgical excision, including ligation of the IMA, he made an uneventful recovery.

Comment

We have presented 2 cases of false aneurysm of the IMA, which appears to be a rare complication of repair of median sternotomy. We have only been able to identify 1 other case of false aneurysm of the IMA associated with sternotomy [2]. In that case there was a sternal wire intimately associated with the false aneurysm. A case of

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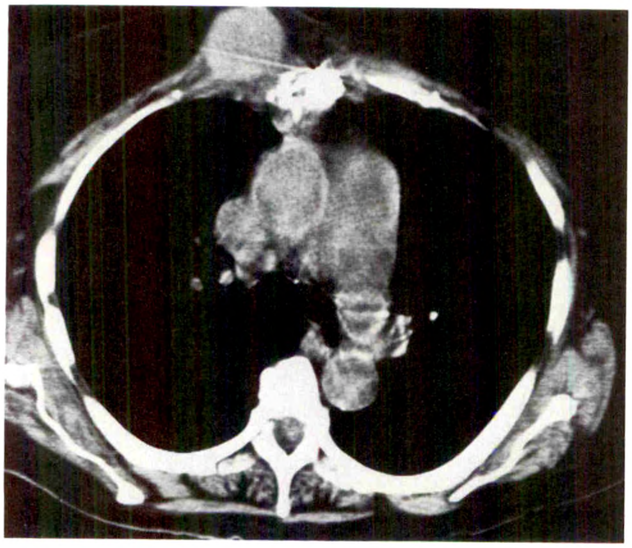

Fig 1. (Patient 1.) Contrast-enhanced thoracic computed tomographic scan. Mass lies anterior to sternum on the right side.

aneurysm of an intercostal artery after repeated needle aspiration of a pleural collection has been reported [3].

It must be presumed that operative trauma was the initiating factor for the formation of the false aneurysm in both our patients. In view of the number of sternotomies performed it is surprising that this is such a rare complication. The absence of a sternal wire in the space and the fact that both of these were right-sided IMA lesions would suggest that a wire had been passed into the space from below into the artery and then withdrawn. In our first patient spontaneous thrombosis of the false aneurysm occurred between the computed tomographic scan and the ultrasound scan; this explains the inability of subsequent angiography to demonstrate the lesion. This was presumably a chance event. As the aneurysm expanded anteriorly and there was not any radiographic evidence of intrathoracic bleeding, it is unlikely that the hypovolemic episodes occurring on the night of the operation were due to bleeding at this site. Although the IMA angiogram was normal, and clinically the false aneurysm had thrombosed, excision biopsy was undertaken in the first patient both to confirm the diagnosis and to allay the patient's anxiety.

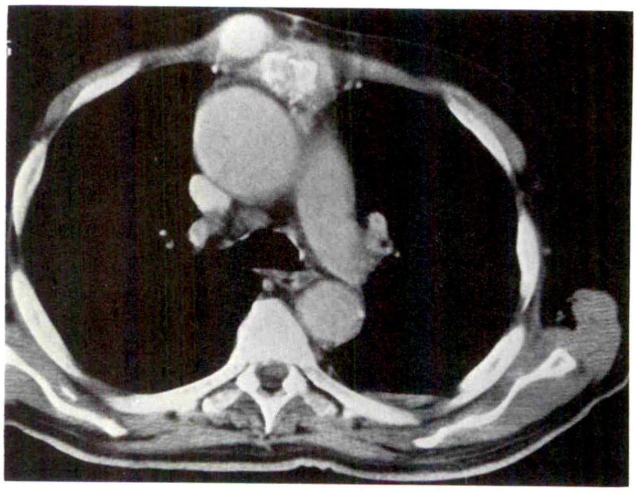

Fig 2. (Patient 2.) Contrast-enhanced thoracic computed tomographic scan. Mass lies anterior to sternum on the right side.

In the second patient the diagnosis was made at surgical exploration; however, if a similar case were to be seen again, we would undertake aortography before operation.

References

1. Martin A, Ross BA, Braimbridge MV. Peristernal wiring in closure of median sternotomy. J Thorac Cardiovasc Surg 1973;66:145–6.
2. Serry C, Bleck PC, Javid H, et al. Sternal wound complications. J Thorac Cardiovasc Surg 1980;80:861–7.
3. Elkington JS, Howell JBL. Aneurysm of an intercostal artery after paracentesis thoracis. Thorax 1960;15:266–7.

Agglutination of Blood Cardioplegia by Cold-Reacting Autoantibodies

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Cold-reacting autoantibodies occasionally occur in patients requiring cardiac operations. This report describes the clinical course of 1 patient with cold-reacting autoantibodies and intracoronary agglutination of the blood cardioplegia solution. Observations made in vivo and in vitro are considered in discussing recommendations for the management of extracorporeal circulation and cardioplegic arrest in patients with clinically silent cold-reacting autoantibodies.

(Ann Thorac Surg 1991;51:833–6)

Cold-reacting autoantibodies are usually of the immunoglobulin M class and are most commonly directed against the human erythrocyte I antigen. Patients with cold-reacting autoantibodies may show the development of acrocyanosis, severe hemolytic anemia, and hemoglobinuria after exposure to cold temperatures; however, cold-reacting autoantibodies with low thermal amplitude are usually clinically silent and may only be detected by preoperative blood typing [1]. The management of patients with cold-reacting autoantibodies who are exposed to hypothermic extracorporeal circulation remains controversial [2–8]. This report describes the clinical course of 1 patient who had cold-reacting autoantibodies with resultant intracoronary agglutination of the blood cardioplegia solution. Our in vivo and in vitro observations serve as the basis for a discussion of existing protocols for the treatment of similar patients.

Case History and In Vitro Observations

The patient is a 69-year-old man with severe pulmonary dysfunction and class IV angina pectoris who was referred for bypass grafting of a proximal stenosis in the anterior descending artery. Angioplasty of this long lesion spanning a large first diagonal branch was considered unsafe.

Extracorporeal circulation was conducted at 28°C and a flow of $1.8\ L \cdot min^{-1} \cdot m^{-2}$. The heart was arrested using a 4°C blood cardioplegia solution. Agglutinated blood was found when the anterior descending artery was incised. Two proximal and two distal saphenous vein anastomoses were constructed during a 38-minute ischemic interval. Rewarming to 37°C was initiated during the last proximal anastomosis. The postcardioplegia reperfusion of the heart was begun with a blood cardioplegia solution delivered at 37°C under controlled conditions of flow and pressure.

Postoperatively there was no grossly evident hemolysis and no inotropic support was required. There was no evidence for myocardial necrosis by serial electrocardiographic or creatine kinase isoenzyme determinations (postoperative total creatine kinase: 76, 380, 227 U/L; creatine kinase-MB: 5, 11, 5 U/L). The patient's subsequent convalescence was uneventful.

In vitro mixing of the patient's blood with cold cardioplegia solution (4°C, 15 minutes) resulted in agglutination (Fig 1). Warming the agglutinated blood to 37°C resulted in dispersion of the erythrocytes (Fig 2). Further agglutination of the patient's blood occurred with continued hypothermia (Fig 3). Subsequent analysis showed that the patient was blood type A Rh+ with an anti-I cold agglutinin titer of 1:256 at 4°C. The patient's blood agglutinated at 24°C (titer, 1:4) but not at 30° or 37°C. The direct antiglobulin test was negative using polyspecific antiglobulin serum, as well as nonspecific anti–immunoglobulin G and anticomplement serum.

Additional in vitro tests were performed to better understand the effect of agglutination on erythrocytes passing through small-caliber conduits. Serum from 3 patients with anti-I titers ranging from 1:4 to 1:32 at room temperature was mixed with red cells and incubated at room temperature and 4°C for 30 minutes. 1+ to 4+ visual agglutination was demonstrated before passing the agglutinated blood through an 18-μm filter (Hemonate-filter, Gesco International Medical, San Antonio, TX). Sixty millimeters of mercury pressure was constantly applied to the agglutinated blood as it passed through the filter by the attachment of a pressurizing syringe to a sphygmomanometer. The blood passed through the filter without hemolysis as determined by testing a 1:100 dilution of serum with an Ames Bililabstix (Miles Inc, Ames Division, Elkhart, IN). Anti-Lewis b reagent antiserum, another cold-reacting antibody, was mixed with Lewis b positive cells and subjected to the same procedure without evidence of hemolysis. Finally, serum from a patient with clinically severe hemolytic agglutinin disease was mixed with adult red blood cells (incubated for 30 minutes at 4°C

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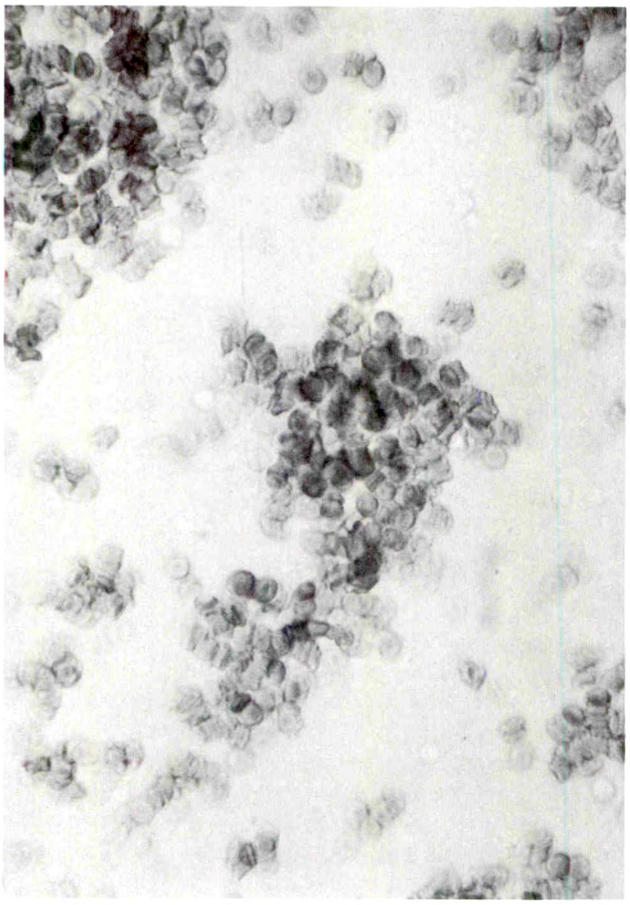

Fig 1. Agglutination of the patient's blood by hypothermia at 4°C for 15 minutes (×100 before 30% reduction.)

and room temperature). A portion of these samples was passed through the same test system. A large amount of hemolysis was demonstrated in all samples. The mechanism for red cell destruction for this in vitro test was therefore complement activation by cold-reacting autoantibodies rather than agglutination and mechanical destruction.

Comment

Our comments are confined to the management of perfusion and hypothermic cardioplegic arrest in patients with the clinically silent, low thermal amplitude, nonhemolytic (ie, benign) variety of cold-reacting autoantibodies. Agglutination of the blood cardioplegia solution in our patient did not cause any discernable myocardial damage, and exposure of the blood to temperatures below 24°C during the initial phases of cooling (water bath = 4°C) did not cause hemolysis or malfunction of the hollow-fiber oxygenator (Bentley BCM-7). The cold-reacting autoantibody in this case caused intracoronary agglutination of the blood cardioplegia solution; however, adverse clinical sequelae of hemolysis or myocardial necrosis did not occur. The agglutination of erythrocytes by antibody probably did not result in capillary occlusion even at temperatures well below the thermal amplitude of the antibody. It is possible that the transcapillary perfusion pressure caused disaggregation of the erythrocytes or that disaggregation occurred with rewarming before the onset of irreversible myocardial ischemic injury.

Warm (23°C) cardioplegic arrest [8], preoperative plasma exchange [4, 8], intraoperative blood exchange [5], and infusion of warm nonoxygenated crystalloid cardioplegia followed by cold crystalloid cardioplegia infusion [3, 5, 7, 8] have all been used in patients with a preoperative finding of cold-reacting autoantibodies. These interventions are intended to decrease the titer of the cold-reacting antibody and maintain the patient's temperature above the thermal amplitude of the antibody. Such interventions may be crucial in patients with complement-fixing antibodies that can cause hemolysis; however, the observations in our case question the necessity for these interventions in patients with clinically silent nonhemolytic cold-reacting autoantibodies.

Although a single infusion of agglutinated blood cardioplegia did not cause myocardial injury in this case, a second infusion of cold (4°C) blood cardioplegia cannot be considered safe in the absence of more complete data. The in vivo and in vitro observations of this report predict that subsequent infusions of cold (4°C) crystalloid cardioplegia solution would be safe if the duration of the procedure

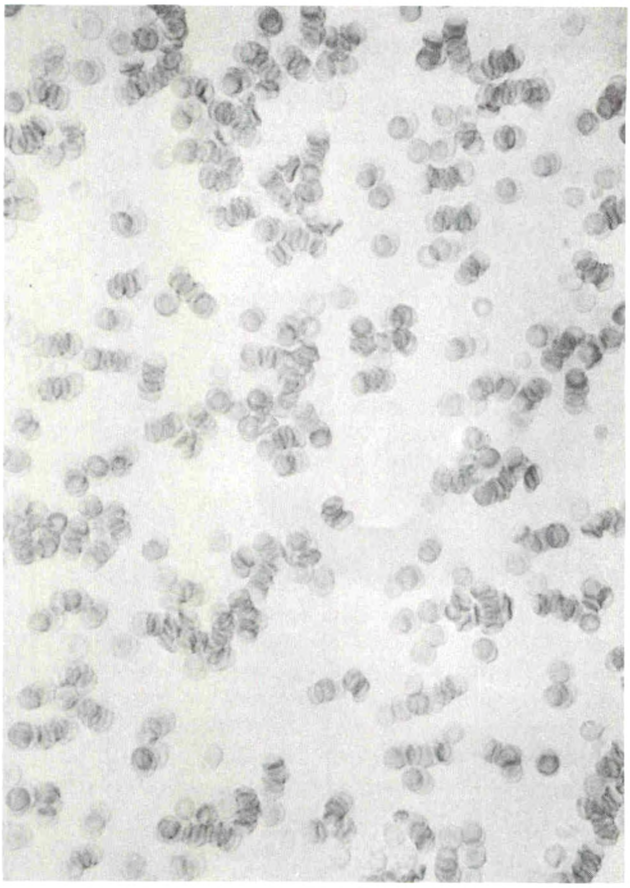

Fig 2. Dispersion of patient's blood by rewarming at 37°C for 15 minutes (×100 before 30% reduction.)

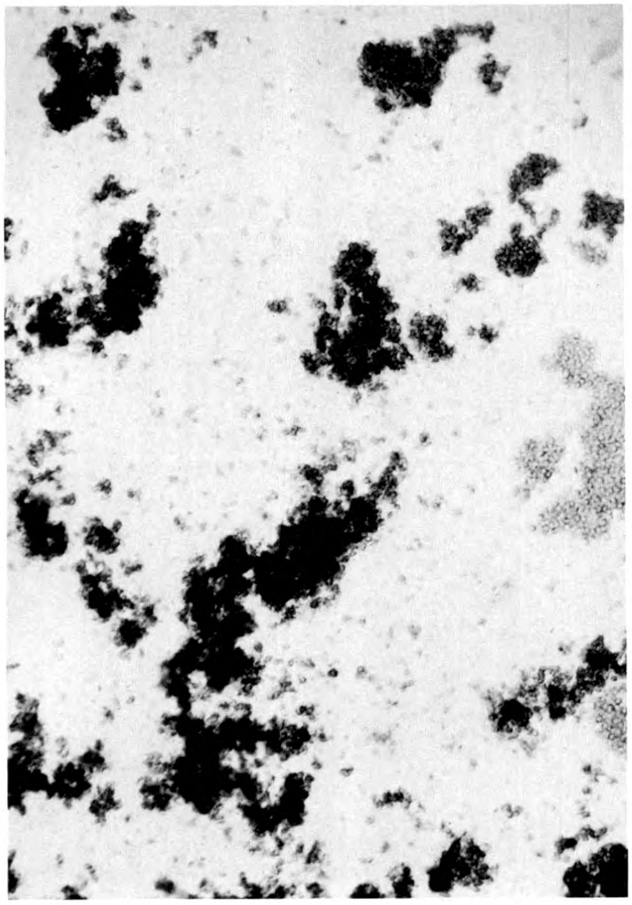

Fig 3. Further agglutination of the patient's blood by continued hypothermia for 30 minutes (×40 before 30% reduction.)

warrants additional doses of cardioplegia. If the presence of nonhemolytic cold-reacting autoantibodies is detected before operation, our experience suggests that 4°C crystalloid cardioplegia could be used safely. The risks of infection and destabilizing fluid shifts associated with plasma exchange are probably not justified in patients with benign cold-reacting autoantibodies.

References

1. Pruzanski W, Shumak KH. Biologic activity of cold-reacting autoantibodies. N Engl J Med 1977;297:538–42, 583–9.
2. AuBuchon AJ, Stofan BA, Davey RJ. Hemolysis during extracorporeal circulation: significance of cold-reactive auto-antibodies and mechanical trauma. Blood 1983;62(Suppl 1):42a.
3. Shahian DM, Wallach SR, Bern MM. Open heart surgery in patients with cold-reactive proteins. Surg Clin North Am 1985;65:315–22.
4. Klein HG, Faltz LL, McIntosh CL, Appelbaum FR, Deisseroth AB, Holland PV. Surgical hypothermia in a patient with a cold agglutinin. Management by plasma exchange. Transfusion 1980;20:354–7.
5. Lee MC, Chang CH, Hsieh MJ. Use of a total wash-out method in an open heart operation. Ann Thorac Surg 1989;47:57–8.
6. Moore RA, Geller EA, Mathews ES, Botros SB, Jose AB, Clark DL. The effect of hypothermic cardiopulmonary bypass on patients with low-titer, nonspecific cold agglutinins. Ann Thorac Surg 1984;37:233–8.
7. Berreklouw E, Moulijn AC, Pegels JG, Meijne NG. Myocardial protection with cold cardioplegia in a patient with cold agglutinins and hemolysins. Ann Thorac Surg 1982;33:521–2.
8. Paccagnella A, Simini G, Nieri A. Cardiopulmonary bypass and cold agglutinin [Letter]. J Thorac Cardiovasc Surg 1988;95:543.

INVITED COMMENTARY

Patients with cold-reacting antibodies are theoretically at risk for hemolysis or microvascular obstruction by red cell aggregates when hypothermic techniques, including cold cardioplegia, are employed during open heart operations. The degree of antibody-mediated hemolysis that occurs in vivo depends on the extent of complement activation. Complement activation through to C3d will result in normal cell survival, activation to C3b will result in extravascular hemolysis, and activation to C9 will result in intravascular hemolysis. Overt hemolysis is unusual, probably as a result of natural inhibitors of the complement cascade. The incidence of microvascular obstruction by red cell aggregates is not known but may be underestimated. For example, red cell aggregates in the coronary circulation after infusion of cold blood cardioplegia might interfere with cardioplegia distribution, leading to poor myocardial protection and depressed left ventricular function. The relationship of these complications to cold agglutinins may not be recognized.

In this case report by Holman and associates, two factors served to mitigate against the development of these complications, even in the presence of gross erythrocyte agglutination. First, the antibody was of low thermal amplitude and midrange titer. Second, the patient had limited coronary disease and the period of systemic and cardiac hypothermia was limited. The favorable outcome in this report cannot necessarily be extrapolated to patients with complex multivessel disease who may require a prolonged hypothermic period.

We also have several reservations about the in vitro methodology employed by Holman and associates. First, there is no evidence that the lack of mechanical trauma to agglutinated red cells when passed through an 18-μm filter under 60 mm Hg pressure accurately simulates the passage of red cells through the coronary microcirculation. Second, the absence of in vitro hemolysis in the three sera tested may be a function of the activity of complement in their test system and may not reflect what would have occurred in vivo. Finally, we are curious as to why the patient's own blood was never subjected to the in vitro testing described.

What then should be the approach to patients with cold agglutinins who undergo coronary operations? Routine preoperative cold temperature screening of all patients' sera is probably not justified owing to the lack of serious clinical sequelae in most instances. For patients undergoing elective procedures who have known potent cold agglutinins, the thermal amplitude and titer of the antibody should be determined. Knowledge of the thermal amplitude can allow the surgeon to control the degree of autoagglutination by manipulation of cardiac, systemic, and infusate temperatures. More complex preoperative and intraoperative techniques should be reserved for the rare patient with the syndrome of cold autoimmune hemolytic anemia. When red cell agglutination is encountered unexpectedly, the following suggestions may be useful: (1) verification by the blood bank that a cold agglutinin and not an unrecognized alloantibody is present; (2) the use of crystalloid cardioplegia to dilute the titer of antibody in the coronary circulation; (3) the use of noncardioplegic techniques; (4) maintenance of systemic temperature greater than 28° to 30°C, at which levels significant agglutination is unlikely to occur; and (5) vigilant inspection of the extracorporeal circuit and oxygenators for aggregates.

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REVIEW OF RECENT BOOKS

AIDS and Surgery

Edited by Andrew J. W. Sim and Donald J. Jefferies
London, Blackwell Scientific Publications, 1990
142 pp, illustrated, $54.95

Reviewed by Carey P. Page, MD

The authors of this 1990 publication have collated the proceedings from a 1987 conference entitled AIDS and Surgery. It represents a "snapshot" of the thoughts and recommendations of scientists and practitioners from the UK and the USA on dealing with a myriad of human immunodeficiency virus (HIV) infection-related issues. Though some of the information is dated, most remains quite applicable and timely. The book is concise and readable. Particularly strong chapters include those concerning the virology of HIV and laboratory and prognostic tests, sterilization and disinfection of equipment including fiberoptic devices, and HIV as an occupational hazard to surgeons. The chapter concerning the legal aspects of acquired immunodeficiency syndrome (AIDS) is as disappointing as the current laws in the UK and USA.

The term *AIDS* (only a portion of the spectrum of HIV infection) and *HIV infection* are used with approximately equal frequency in this book. This refreshing change is perhaps evidence of maturation of our collective thought processes and similar to transitionally discarding the term *consumption* once we had a clearer understanding of the bacteriology, epidemiology, and control of tuberculosis. This transition reminds all readers new to the area that the true extent of the current epidemic and the real occupational risks are reflected by HIV-infected individuals—not just those with full-blown AIDS.

Because the editors ". . . have altered the manuscripts as little as possible, . . . individual authors' approaches (and attitudes) . . . permeate the text." The professional and ethical conflicts engendered by governmental policies of treating HIV infection and HIV-related illness as social problems rather than as a fatal infectious disease are readily apparent throughout the book, both by direct comment and through inference. Among these conflicts is the impediment to infection control, public health, and occupational risk identification imposed by undue emphasis on individual rather than societal rights. Also evident is the paradox between that which seems medically and epidemiologically sound and that which is "legal."

This book should be mandatory reading for two identifiable groups of surgeons: (1) "those who either ignore or do not believe there are aspects of surgery which will be affected by HIV infection" and (2) "those who take an active stance and refuse to operate on any individual who carries or might carry the virus." It will be a welcome source of information to "those surgeons who recognize that HIV infection will be with us for the foreseeable future, that there are risks involved, and that *something* can be done to reduce the chance of occupational infection."

San Antonio, Texas

Blast Injury to the Thoracic Esophagus

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Blast injury causing pneumatic disruption of the esophagus is a rare and potentially lethal injury. The mortality and morbidity rates are high unless the injury is promptly recognized and treated. Our experience with a midesophageal perforation resulting from a blast injury emphasizes the importance of awareness of this condition and of the chest radiograph in making an early diagnosis.

(Ann Thorac Surg 1991;51:837–9)

Esophageal rupture carries a mortality rate of approximately 30% [1]. Most esophageal ruptures result from iatrogenic causes. Rarely does blunt trauma result in isolated esophageal rupture. One unusual form of esophageal rupture is that resulting from accidental discharge of gas under pressure into the oral cavity. In this report we describe a recent case of a midesophageal rupture after the explosion of a compressed air tank. A review of the literature documents that the diagnosis is often missed or delayed with resulting increased morbidity and mortality. Awareness of this unusual situation and close attention to the findings on the chest radiograph are necessary for prompt diagnosis.

A compressed air tank exploded directly in front of a 35-year-old construction worker. He was struck in the face by a piece of metal and knocked off an 8-foot-high platform by the blast.

When seen at the hospital the patient was not dyspneic and had stable vital signs. An initial supine chest radiograph was reported as normal. The patient was taken to the operating room for debridement and repair of orbital and maxillary fractures.

Postoperatively he complained of increasing dyspnea, and a chest radiograph in the upright position showed a small right hydropneumothorax. This was promptly treated by tube thoracostomy. Twelve hours later, the chest tube began to drain large volumes of frothy fluid.

Because of the foul nature of the drainage and the suspicion of a blunt injury to the cervical or thoracic esophagus, an urgent esophagogram using water-soluble contrast medium was done. The study showed a large extravasation of contrast material into the right pleural space with no definite site of esophageal disruption. In the operating room rigid esophagoscopy was performed, which demonstrated only mucosal hemorrhage and edema in the midthoracic esophagus. A right posterolateral thoracotomy was then performed, which disclosed disruption of the right mediastinal pleura and a longitudinal rupture of the midthoracic esophagus just distal to the azygos vein and extending 6 cm. The edges of the mucosa were smooth, and a marked inflammatory reaction was present in both the mediastinum and pleural space. The longitudinal rupture was primarily closed with multiple interrupted sutures of 3-0 Dexon and the repair was buttressed with a large parietal pleural flap as described by Michel and Grillo [2]. The mediastinum was left open. The pleural space was drained with three chest tubes. A laparotomy was then performed for a gastrostomy and feeding jejunostomy.

Postoperatively, increasing respiratory insufficiency with bilateral pulmonary infiltrates developed, necessitating tracheostomy and prolonged ventilatory support. Pulmonary insufficiency was originally attributed to contusion from the blast injury, but in retrospect the patient's prolonged course is more consistent with adult respiratory distress syndrome secondary to sepsis from extensive mediastinal soilage.

An esophagogram using water-soluble contrast medium 10 days after esophageal repair showed a small leak from the midthoracic esophagus promptly drained by the posterior chest tube. Gradually, with prolonged pleural and gastric drainage as well as enteral nutrition by jejunostomy, the fistula closed. He was discharged home 4 weeks after injury.

Comment

Although traumatic perforations figure largely in the recent series of esophageal perforations, pneumatic perforation is rarely mentioned [2–4]. Of 231 reported cases of esophageal perforations, only 1 was the result of a blast injury. Only 18 cases of pneumatic disruption of the esophagus have appeared since Petrin's [5] original report, in which he describes a fatal distal esophageal rupture after the accidental discharge of a compressed air hose into the mouth of a 27-year-old man. The mechanism of injury in all 18 cases of blast rupture of the esophagus appears to be the same. A blast of compressed air directed into the pharynx of the victim results in rapid distention of the pharynx and respiratory passages.

The pressure necessary to cause esophageal rupture has been studied experimentally. Kinsella and associates [6] and Mackler [7] produced experimental rupture of the esophagus with an average pressure of 5 psi. The lower end of the esophagus is anatomically the weakest portion of this organ, and consequently, the majority of sponta-

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Table 1. Cases of Blast Injury to the Thoracic Esophagus

Reference	No. of Cases	Mechanism of Injury	Site	CRX	Pneumothorax	Pneumomediastinum	Cervical Emphysema	SC Emphysema
Michel et al [2]	1	Compressed air	Lower	[a]				
Petrin [5]	1	Compressed air hose	Lower	[a]		+		
Borghero [11]	1	Compressed gas	Lower	+	+			
Kerr et al [12]	1	Child bit inner tube	Lower	+	+	+		+
Volk et al [13]	1	Compressed air tank	TE fistula	+	+			
Hood [14]	1	Compressed air	Cervical	+		+	+	
Webster and Taylor [15]	1	Compressed air	Cervical	+				
Holaday [16]	1	Compressed air	Lower	+		+		
Cole and Burcher [17]	1	Fire extinguisher	Lower	+	+	+		
Levy and Thomas [18]	1	Compressed air	. . .	[a]				
Randolph et al [19]	1	Child bit inner tube	Lower	−				+
Hendricks and Barnes [20]	1	Exploding tire	Middle	+		+		
Bradruddoja and MacGregor [21]	1	Exploding tire	Upper	+	+	+		
Buntain and Lynn [22]	1	Child bit inner tube	Lower	+	+	+		
Gelfand et al [23]	1	Child bit inner tube	Lower	+	+			
Conlan et al [24]	1	Soda bottle	Cervical	+		+	+	
Love and Berkow [9]	1	Soda bottle	Lower	+		+	+	
Hainsworth [25]	1	Compressed air	Middle	+	+		+	
Guth et al (present report)	1	Compressed air	Middle	+	+			+

[a] Not reported in discussion.

CRX = chest roentgenogram; SC = subcutaneous; TE = tracheoesophageal.

neous ruptures occur in the distal third; rupture of the upper thoracic esophagus, however, is not unknown. Bates [8] reported 4 cases of pressure rupture of the midthoracic esophagus. Blast injury can affect any site along the length of the esophagus; reported sites range from the cervical esophagus with concomitant tracheoesophageal fistula to the more common rupture of the distal third of the thoracic esophagus.

Early diagnosis of esophageal rupture is of vital importance. In the reported series of spontaneous perforations of the esophagus by blunt injury, those patients who died had an average delay of 30 hours; delay averaged only 8 hours in survivors. In our case, the correct diagnosis was only made 24 hours after the original injury. A high index of suspicion is essential to promptly detect esophageal perforations. The condition should be considered in any patient with a sudden onset of dyspnea and chest pain after any event that could lead to an unusual increase in intrathoracic pressure. Subtle abnormalities in the chest radiographs can suggest the diagnosis and localize the site of injury [9, 10]. Cervical perforations often have as signs subcutaneous emphysema and anterior displacement of the trachea. Rupture of the thoracic esophagus is accompanied by mediastinal widening with emphysema and often a hydropneumothorax. At least one of these findings was described in all but 2 cases from the literature review (Table 1). Thus, hydropneumothorax on a chest radiograph in a trauma patient without penetrating trauma or rib fractures should be promptly evaluated with an esophagogram to exclude a ruptured esophagus.

Buttressed primary repair of the injury is the treatment of choice. Early diagnosis and treatment by debridement, wide drainage, primary buttressed repair, and nutritional support offers the best chance for these patients. This approach can be applied to all cases whether the diagnosis is made early or late.

In summary, pneumatic rupture of the esophagus is a lethal condition. A history of external barotrauma should prompt a vigorous search for the evidence of esophageal perforation. The presence of a pneumothorax, pneumomediastinum, or crepitus on physical examination indicates esophageal perforation. A prompt radiographic contrast study will confirm the diagnosis. Appreciation of the early clinical and radiographic findings of pneumatic rupture of the esophagus is essential for prompt diagnosis and successful therapy.

References

1. Loop FD, Groves LK. Esophageal perforations. Ann Thorac Surg 1970;10:571–87.
2. Michel L, Grillo H, Malt R. Operative and nonoperative management of esophageal perforations. Ann Surg 1981;194:57–63.

3. Nesbitt J, Sawyers J. Surgical management of esophageal perforations. Am Surg 1987;53:184–91.
4. Goldstein L, Thompson W. Esophageal perforations: a 15 year experience. Am J Surg 1982;143:495–503.
5. Petrin G. Ein Fal von traumatischer Oesophagusruptur nebst Bermerkugen uber dei Entstehung der Oesophagusrupturen. Beitr Klin Chir 1909;61:265–84.
6. Kinsella TJ, Morse RW, Hertzog AJ. Spontaneous rupture of the esophagus. J Thorac Surg 1984;17:613–31.
7. Mackler SA. Spontaneous rupture of the esophagus: an experimental and clinical study. Surg Gynecol Obstet 1952; 95:345–56.
8. Bates M. Pressure rupture of the mid thoracic esophagus. Br J Surg 1969;56:327–31.
9. Love L, Berkow AE. Trauma to the esophagus. Gastrointest Radiol 1978;2:305–21.
10. Phillips LG, Cunningham J. Esophageal perforation. Radiol Clin N Am 1984;22:607–13.
11. Borghero A. Un eccezionale de caseo di rottura dell' esofago da penetrazione accidentale di gas compresso (metano) attraverso la cavita' orale. Riv Infort Mal Profes 1953;40:860–6.
12. Kerr HH, Sloan H, O'Brien CE. Rupture of the esophagus by compressed air. Surgery 1953;33:417–20.
13. Volk H, Storey CF, Marrangoni AG. Tracheo-esophageal fistula by compressed air. Surgery 1953;40:860–6.
14. Hood RM. Rupture of the esophagus by compressed carbon dioxide. US Armed Forces Med J 1957;8:587–90.
15. Webster PD, Taylor JR. Traumatic rupture of the esophagus by compressed air. NC Med J 1957;18:305–11.
16. Holaday WJ. Rupture of the esophagus by compressed air. N Engl J Med 1959;261:1071–3.
17. Cole DS, Burcher SK. Accidental pneumatic rupture of the stomach and esophagus. Lancet 1961;1:24–5.
18. Levy SJ, Thomas G. Partial rupture of the esophagus due to compressed air. Proc Mine Med Off Assoc 1966;46:59.
19. Randolph H, Melik DW, Grant AR. Perforation of the esophagus from external trauma or blast injuries. Dis Chest 1967; 51:121–4.
20. Hendricks GL, Barnes WT. Accidental rupture of the esophagus by compressed air. Ann Thorac Surg 1971;12:437–41.
21. Bradruddoja M, MacGregor JK. Rupture of the intrathoracic esophagus by compressed air blast. Arch Surg 1971;103: 417–9.
22. Buntain WL, Lynn HB. Traumatic pneumatic disruption of the esophagus. J Thorac Cardiovasc Surg 1972;63:553–60.
23. Gelfand ET, Fisk LR, Callaghan JC. Accidental pneumatic rupture of the esophagus. J Thorac Cardiovasc Surg 1977;74: 142–4.
24. Conlan AA, Wessels A, Hammond CA, Beale PG, Katz G. Pharyngoesophageal barotrauma in children: a report of six cases. J Thorac Cardiovasc Surg 1984;88:452–3.
25. Hainsworth PJ. The dangers of home-brewing: oesophageal rupture. Br J Surg 1987;74:151.

The European Association for Cardio-Thoracic Surgery Notice of Annual Meeting

The Fifth Annual Meeting of the European Association for Cardio-Thoracic Surgery will be held September 22–25, 1991, at the Royal Lancaster Hotel in London, United Kingdom. The scientific sessions are open to all registered participants. The registration fee includes admission to the entire scientific program, meeting documentation, welcome reception on Sunday evening, concert on Monday evening, and tea and coffee.

Registration and Hotel Reservation

All participants of the meeting should request a registration form from Conference Associates & Services Ltd, EACTS, Congress House, 55 New Cavendish St, London W1M 7RE, United Kingdom (telephone: 071 486 0531; facsimile: 071 935 7559).

Pericardial Cyst With Partial Erosion of the Right Ventricular Wall

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A case of pericardial cyst with partial erosion into the anterior wall of the right ventricle is presented. Cardiopulmonary bypass was necessary for excision of the cyst. This report helps to alert surgeons of the possible need for cardiopulmonary bypass during the removal of some pericardial cysts, especially in patients with signs and symptoms of infection and in whom preoperative imaging fails to show distinct margins between the cyst and cardiac structures.

(Ann Thorac Surg 1991;51:840–1)

Congenital pericardial cysts are most often asymptomatic and are usually discovered as an incidental finding on routine chest roentgenography. They are generally believed to follow a benign course in the majority of cases. Complications of these cysts have been reported in the literature and include cyst rupture [1], compression of the heart with alteration in hemodynamics [2, 3], and compression of the right main bronchus [4]. This report documents a case of a pericardial cyst associated with persistent high fevers that was, at operation, found to be eroding into the anterior wall of the right ventricle.

A 21-year-old man was referred to us because of recurrent chest pain, fever, and an intrapericardial mass. This patient was known to have a mediastinal mass since he was 13 years old, when a chest roentgenogram taken to evaluate symptoms of cough and low-grade fever showed the abnormality. He underwent an exploratory right thoracotomy, but the mass was not removed because it was noted to be densely adherent to the heart. A cardiac catheterization was attempted but was aborted because the patient reportedly had an anaphylactic reaction to the intravenous contrast medium. However, a right atrial injection failed to show any communication between the mass and the right atrium or the ventricle. In subsequent years, serial echocardiograms showed that the mass was stable in size. During this time, the patient experienced occasional episodes of cough and low-grade fever that were often treated with oral antibiotics.

On admission to the referring hospital, the physical examination was remarkable for a temperature of 40°C but was otherwise normal. The white blood cell count was 13.9×10^9/L (13,900/μL), and blood cultures were positive for group B streptococcus. The erythrocyte sedimentation rate was 56 mm/h. The patient was started on a therapeutic regimen of intravenous antibiotics. A chest roentgenogram showed a large anterior mediastinal mass but no other abnormalities (Fig 1). A computed tomographic scan of the chest showed a bilobed cystic mass measuring 12 cm in the greatest dimension situated within the pericardium. The mass was overlying both the right atrium and right ventricle, and a clear margin between the mass and the right ventricular wall could not be discerned (Fig 2). A catheterization of the right and left sides of the heart with right atrial contrast injection and coronary arteriography was performed after premedication and intravenous steroids were given, and the procedures showed no communication between the mass and the cardiac chambers and no evidence for a blood supply to the mass from the coronary arteries. Marked extrinsic compression of the right atrium and the right ventricle was evident.

The patient was treated with intravenous antibiotics for 10 days but had persistent fever and complained of constant retrosternal pain. Two subsequent white blood cell counts remained elevated and the erythrocyte sedimentation rate had increased to 96 mm/h. Because of a persistent febrile course despite adequate antibiotic therapy, and continuous retrosternal pain, the decision was made to explore the mediastinum.

At the time of operation, intraoperative transesophageal echocardiography demonstrated a bilobed, primarily fluid-filled cystic mass along the border of the right side of the heart (Fig 3).

The patient was explored through a median sternotomy. A large cystic mass that was densely adherent to the right ventricular wall was encountered. Cardiopulmonary bypass and cardioplegic arrest of the heart were established before proceeding with excision of the cyst. On opening the cyst, blood and laminated thrombus were encountered. Inspection of the cyst floor showed extensive erosion of myocardial tissue, and the thickness of the ventricular wall was significantly attenuated. The cyst was trimmed, and multiple bleeding points along the cut edges of the cyst were controlled with suture ligatures. The edges were then plicated over the attenuated ventricular wall with pledgeted sutures to reinforce it.

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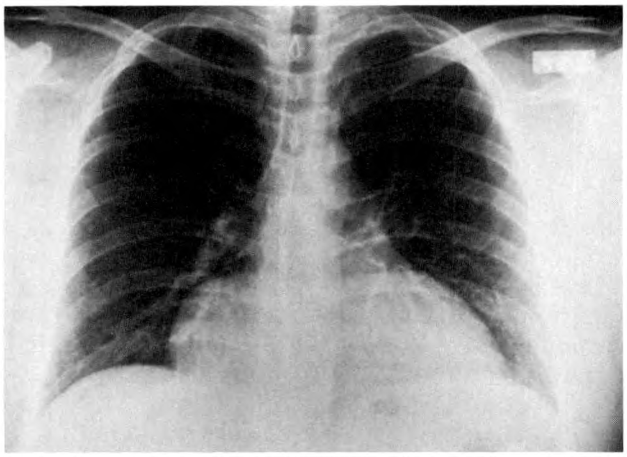

Fig 1. Posteroanterior chest roentgenogram showing a large mediastinal mass.

Pathologic examination of the specimen showed a mesothelial-lined structure overlying a thin layer of fibrous tissue and occasional smooth muscle cells. There were multiple areas of acute and chronic inflammation. Intraoperative cultures were negative. The patient remained afebrile in the postoperative period and his recovery was uneventful. He was discharged on the sixth postoperative day.

Comment

This case illustrates an unusual complication of a pericardial cyst. The association of fever and positive blood cultures and the grossly inflamed condition of the cyst is highly suggestive of bacterial infection of the cyst, though cultures of the cyst and cyst contents were negative. It is possible, with the long-standing history of episodic low-grade fever and cough, that chronic infection of the cyst existed. This would account for the extensive inflammation and erosion into the right ventricular wall that we encountered. The degree of inflammation and attenuation of the right ventricular free wall indicated that rupture of the right ventricle in the cystic mass was imminent.

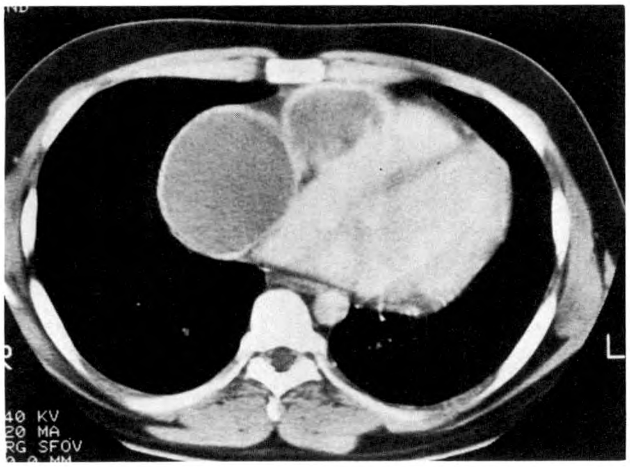

Fig 2. Computed tomogram showing a large bilobed cystic mass. An area with margins that are indistinct from adjacent cardiac structure can be seen.

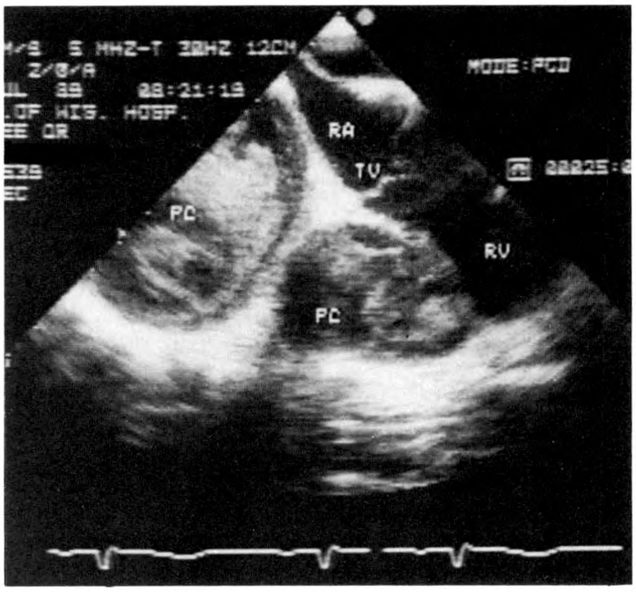

Fig 3. Transesophageal echocardiogram taken at the time of operation. Shown are cross-sections through the two major components of the pericardial cyst (PC). The cyst extends along the free wall of the right atrium (RA), tricuspid valve plane (TV), and the free wall of the right ventricle (RV).

To our knowledge, this is an unusual if not unique case, because cardiopulmonary bypass was necessary for the removal of a congenital pericardial cyst eroding into the right ventricular free wall. Others have reported pericardial cysts intimately associated with the heart causing altered cardiac function purely by compression [2, 3], but successful removal of these cysts could be achieved without cardiopulmonary bypass. In this patient, removal of the cyst followed by adequate evaluation and reinforcement of the thinned ventricular wall could not be accomplished without cardiopulmonary bypass and cardioplegic arrest. We suggest that the surgeon must be aware of the possible need for cardiopulmonary bypass during cyst excision in patients with a pericardial cyst who have signs and symptoms of infection and evidence of erosion into cardiac structures.

References

1. King JT, Crosby I, Pugh D, Reed W. Rupture of a pericardial cyst. Chest 1971;60:611.
2. Engle DE, Tresch DD, Boncheck LI, Foley WD, Brooks HL. Misdiagnosis of a pericardial cyst by echocardiography and computed tomography scanning. Arch Intern Med 1983;143:351–2.
3. Shaver VC, Bailey WR, Marrangoni AG. Acquired pulmonic stenosis due to external cardiac compression. Am J Cardiol 1965;16:256–61.
4. Davis WC, German J, Johnson NJ. Pericardial diverticulum causing pulmonary obstruction. Arch Surg 1960;82:285–9.

Dissectors for Pulmonary Thromboendarterectomy

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Even with circulatory arrest during pulmonary thromboendarterectomy, continued back-bleeding obscures the operative field. This necessitates frequent interruptions of dissection to allow aspiration with a second instrument. Therefore, pulmonary thromboendarterectomy dissectors are described that allow simultaneous suction of blood from the operative field. Before the use of these dissectors, circulatory arrest time was 59 ± 23 minutes in 124 consecutive patients. In the last 10 consecutive patients using these dissectors, the mean circulatory arrest time has been 52 ± 22 minutes (p = not significant). It is anticipated that with a larger database, the ability to aspirate blood simultaneously during the dissecting process will result in a significant shortening of circulatory arrest time.

(Ann Thorac Surg 1991;51:842–3)

Pulmonary thromboendarterectomy has been established as an effective modality for the treatment of patients who are severely disabled from pulmonary hypertension secondary to chronic pulmonary embolism [1]. One method of pulmonary thromboendarterectomy involves the use of multiple periods of circulatory arrest during deep hypothermia [2].

Circulatory arrest is necessary because of continued severe bronchial back-bleeding obscuring the operative field during the process of endarterectomy. Back-bleeding is primarily due to bronchial artery hyperplasia secondary to chronic hypoxemia. Even with circulatory arrest and exsanguination of the patient into the cardiotomy reservoir, back-bleeding continues, albeit in decreased amounts, during the endarterectomy process. There is enough back-bleeding, however, that repeated suctioning is necessary to provide an unobstructed operative field. Furthermore, it has been demonstrated that an increased incidence of postoperative delirium is associated with total circulatory arrest times exceeding 55 minutes [3].

Therefore, in an effort to minimize total circulatory arrest times, we have designed dissectors that simultaneously apply suction at the site of dissection so that it is unnecessary to stop the dissecting process repeatedly and to aspirate blood from the operative field with a separate instrument.

Description of the Dissectors

There are six separate dissectors in a set. The tip consists of a sphere 2 mm in outside diameter and has multiple perforations to allow simultaneous suction during dissection (Fig 1). The overall length of the dissectors is 29.5 cm. The handle portion is 12 cm in length and 0.7 cm in diameter. The distance from the handle to the point of angulation is 12.5 cm. The angles for the dissectors are 0, 30, 45, 60, and 80 degrees. The distance from the angle to the tip is 5 cm. In addition, there is a dissector of 80-degree angulation 3 cm from the angle to the tip. The opening in the end of the handles is 4.4 mm, which is the standard size for an intravenous tubing set. One may connect the dissectors to the cardiotomy reservoir or to a Cell Saver device (Fig 2). The dissectors are illustrated in Figure 3.

Comment

In 124 consecutive patients using dissectors without simultaneous suction capability, the mean circulatory arrest time was 59 ± 23 minutes (standard deviation) (range, 16 to 129 minutes) versus 52 ± 22 minutes (range, 26 to 82 minutes) in the last 10 consecutive patients (p = not significant). However, it is anticipated that with an in-

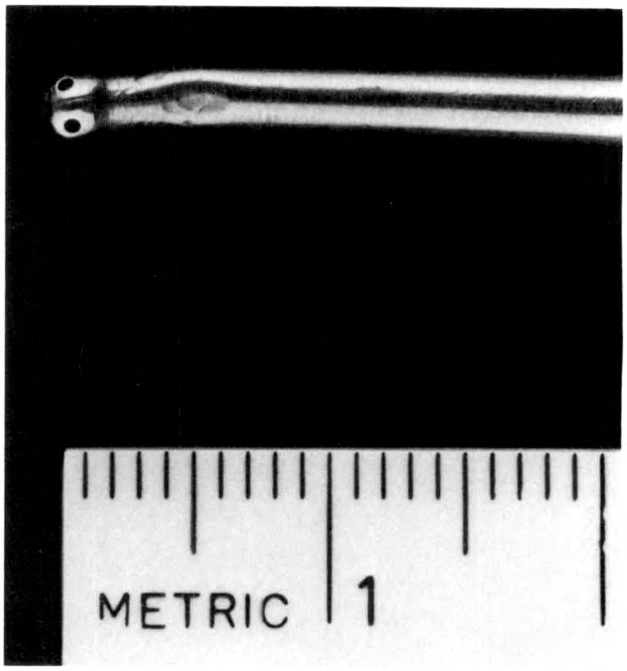

Fig 1. Detail of dissector tips. The dissector tip is spherical and 2 mm in outside diameter. Four holes, 0.5 mm in diameter, are drilled at 90 degrees to each other to permit simultaneous aspiration of blood during dissection.

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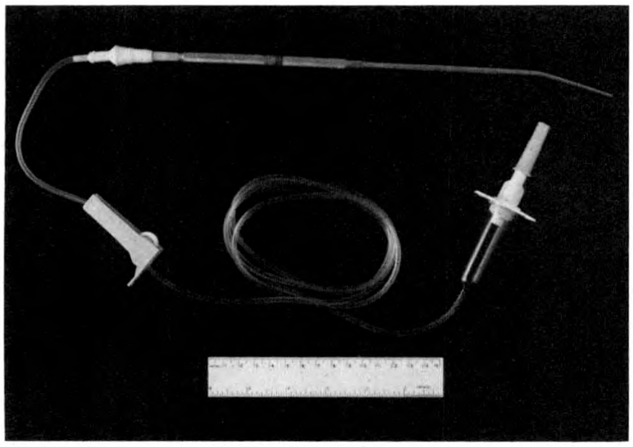

Fig 2. Connection to intravenous tubing. A standard intravenous tubing is inserted into the end of the handle. The opposite end can be connected to wall suction, a Cell Saver device, or cardiotomy suction to conserve blood.

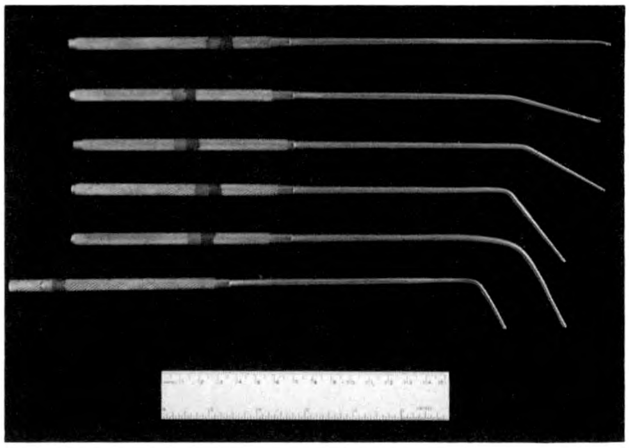

Fig 3. Array of dissectors. The various angles of the dissectors and tip lengths facilitate dissection of all of the bronchopulmonary segmental arteries. The dimensions and angles are described in the text.

creased number of patients in the latter group, the decrease in total circulatory arrest time will reach statistical significance. Consequently, the incidence of postoperative delirium should be lessened. Additionally, total cardiopulmonary bypass time, which has been shown to be related to the necessity for prolonged ventilation postoperatively and operative mortality [4], may be reduced.

References

1. Daily PO, Dembitsky WP, Peterson KL, Moser KM. Modifications of techniques and early results of pulmonary thromboendarterectomy for chronic pulmonary embolism. J Thorac Cardiovasc Surg 1987;93:221–33.
2. Daily PO, Dembitsky WP, Iversen S. Technique of pulmonary thromboendarterectomy for chronic pulmonary embolism. J Cardiac Surg 1989;4:10–24.
3. Wragg RE, Dimsdale JE, Moser KM, Daily PO, Dembitsky WP, Archibald C. Operative predictors of delirium after pulmonary thromboendarterectomy. A model for postcardiotomy delirium? J Thorac Cardiovasc Surg 1988;96:524–9.
4. Daily PO, Dembitsky WP, Iversen S, Moser KM, Auger W. Risk factors for pulmonary thromboendarterectomy. J Thorac Cardiovasc Surg 1990;99:670–8.

Reinforced Sternal Closure

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A technique of reinforced sternal closure with stainless steel struts is described. Stable sternum avoids severe complications such as mediastinitis and sternal dehiscence.

(Ann Thorac Surg 1991;51:844–5)

Median sternotomy is the most common surgical incision used in open heart operations. It consists of a surgical longitudinal fracture and its later correction, which implies some type of orthopedic closure. The usual primary closure is done with interrupted perforating wire stitches. Alternative methods such as interrupted sutures of Teflon-impregnated Dacron [1], Parham bands [2], and Silastic bands [3] have been abandoned.

A special reinforced method of sternal closure should be applied in the following cases: sternal dehiscence, bone fracture, reoperation, obesity, diabetes, bilateral mammary artery dissection for bypass grafting [4], anticipated postoperative low cardiac output, anticipated prolonged respiratory assistance, faulty sternum (very rarely recognized) [5], and hypoplasia of the sternum. Robicsek [6], Sutherland [7], Lambert [8], Di Marco [9], and their associates have published different methods of sternal closure based on the way the wire stitching is done.

We have designed a perforated longitudinal strut of surgical stainless steel. This strut is 22 mm wide and 5 mm thick; its length, which varies according to the patient's characteristics, may be 14, 16, or 18 cm. Its shape is like that of the Greek letter Omega (Ω), and it has holes every 2 cm down the middle (Fig 1).

The strut is placed on the internal side of each half of the divided sternum and then fixed with wire stitches that

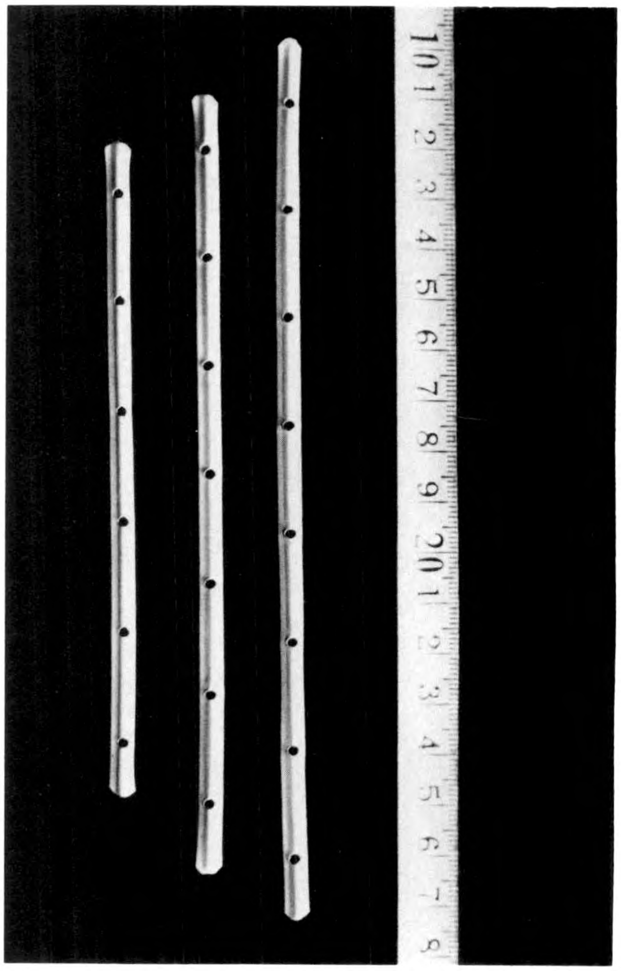
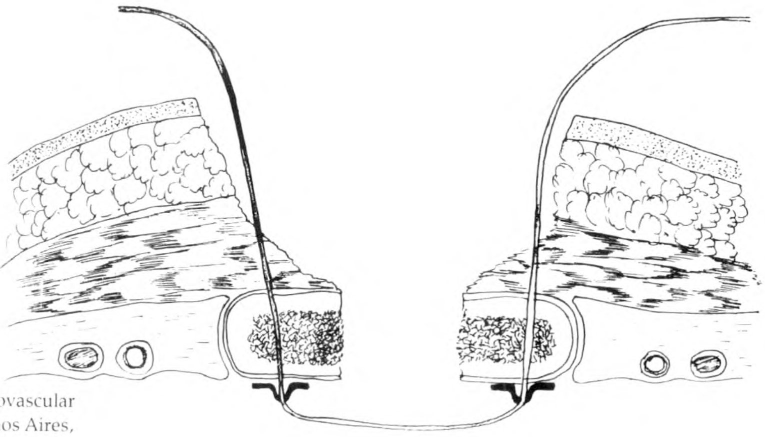


Fig 1. Three sizes of the stainless steel struts.

Fig 2. Struts placed on the internal sides of the divided sternum.



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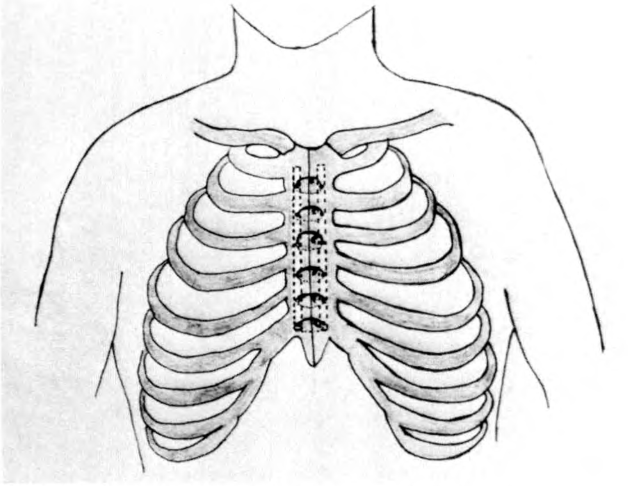

Fig 3. Single stitches through the sternum and struts.

pass through the holes of the strut and the sternum (Fig 2). The wire stitches can be placed as single stitches, U stitches, or figure-of-8 stitches according to what the surgeon considers appropriate and the state of the sternum in each of the previously mentioned particular cases (Fig 3). Finally, they are twisted to secure the stitching. This technique has been applied in several patients, resulting in successful sternal stability (Fig 4).

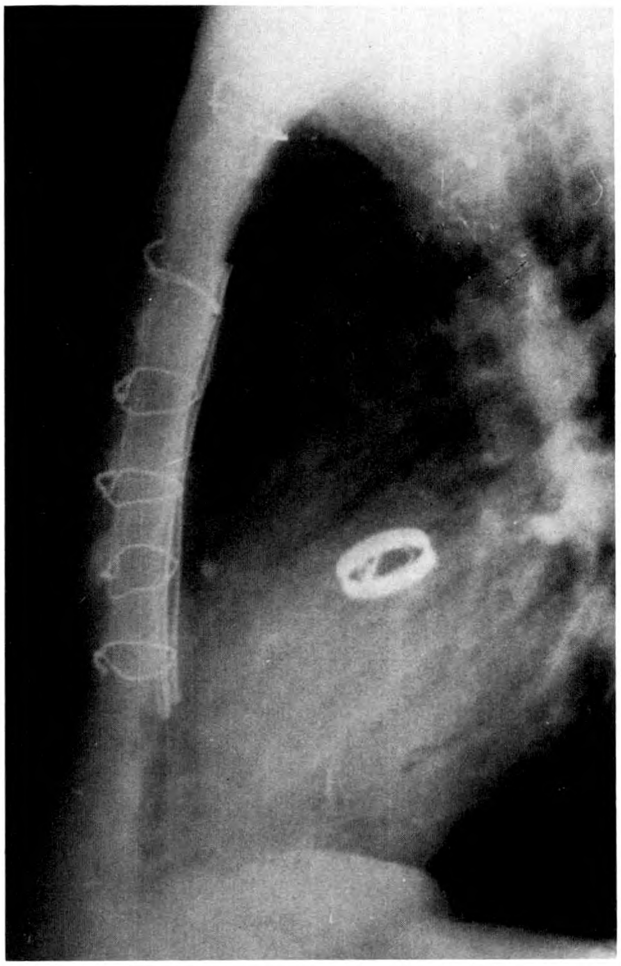

Fig 4. Lateral chest roentgenogram showing struts in place.

References

1. Macmanus Q, Okies JE, Phillips SJ, Starr A. Surgical considerations in patients undergoing repeat median sternotomy. J Thorac Cardiovasc Surg 1975;69:138–43.
2. Okies JE, Phillips SJ. Sternal approximation. Ann Thorac Surg 1974;17:423–4.
3. LeVeen HL, Piccone VA. Nylon-band chest closure. Arch Surg 1968;96:36–9.
4. Loop FD, Lytle BW, Cosgrove DM, et al. Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. Ann Thorac Surg 1990;49:179–87.
5. Shafir R, Weiss J, Herman O, Cohen N, Stern D, Igra Y. Faulty sternotomy and complications after median sternotomy. J Thorac Cardiovasc Surg 1988;96:310–3.
6. Robicsek F, Daugherty HK, Cook JW. The prevention and treatment of sternum separation following open-heart surgery. J Thorac Cardiovasc Surg 1977;73:267–8.
7. Sutherland RD, Martinez HE, Guynes WA. A rapid, secure method of sternal closure. Cardiovasc Dis Bull Tex Heart Inst 1981;8:54–5.
8. Lambert CJ, Mitchel BF, Adam M, Shiekh S. A modified technique for secure median sternotomy closure. Surgery 1971;69:393.
9. Di Marco RF, Lee MW, Bekoe S, Grant KJ, Woelfel GF, Pellegrini RV. Interlocking figure-of-8 closure of the sternum. Ann Thorac Surg 1989;47:927–9.

Simplified Method for Femoral Venous Cannulation

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A simple method for rapidly achieving femoral venous cannulation is described. We have found this method to be particularly useful for femoral cannulation when the patient is in the thoracotomy position.

(Ann Thorac Surg 1991;51:846–7)

Adequate venous drainage for cardiopulmonary bypass is often difficult to achieve through the femoral veins unless the venous cannula is positioned near the right atrium. Passage of large cannulas through femoral and iliac veins is sometimes made difficult by the local anatomy of the venous system, previous operation, webs in the left iliac vein as it crosses under the iliac artery, calcified arteries, and the sacral promontory. Femoral venous cannulation may be particularly difficult when the patient is in the left thoracotomy position as for repair of thoracic aneurysms, reoperative coronary artery bypass grafting [1], or left lung transplantation (if the patient requires pump oxygenator support). The use of a flexible metal obturator such as an endotracheal tube stylet inserted into a venous cannula, allowing it to be preshaped before insertion, has not been uniformly reliable in our hands.

Technique

We have developed a simple method for proper placement of femoral venous cannulas. The femoral vessels are exposed in a routine manner and prepared for cannulation. A venotomy is made and a soft 14F plastic catheter is advanced through the common femoral vein. The 14F catheter must be at least twice the length of the venous cannula to be inserted to avoid loss of the 14F catheter during positioning of the venous cannula. The soft 14F catheter is generally easily manipulated into the inferior vena cava and then into the right atrium, if necessary. A standard single-stage right atrial venous cannula is selected based on the size of the femoral vein to be cannulated. The venous cannula selected should obviously be long enough to reach from the femoral vein insertion site to the inferior vena cava–right atrial junction. Modification of the venous cannula is then performed by cutting a hole in the tip of the cannula so that it may be advanced over the 14F soft plastic catheter and into appropriate position.*

If difficulty is encountered in advancing the 14F soft plastic catheter into the venous system, a long guidewire can first be passed through the femoral venotomy. The 14F catheter can then be easily passed over the wire (Fig 1). We have previously attempted to pass venous cannulas over a guidewire only and have found that the guidewire is too thin and flexible compared with the rigid cannula. As a result, the guidewire usually deforms and does not facilitate passage of the venous cannula. We have found that the 14F plastic catheter, however, guides venous cannulas into position reliably (Fig 2). If difficulty in passing the cannula over the plastic catheter is still encountered, table flexion at the hip is often a helpful maneuver.

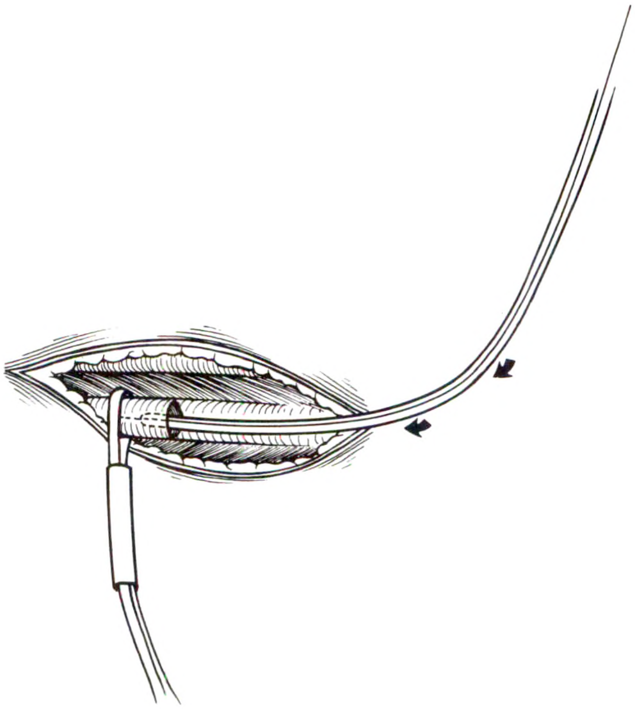

Fig 1. Insertion of the catheter over a guidewire passed into the venous system through a left groin incision.

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* A preassembled catheter, guidewire, and cannula kit is available from Research Medical, Inc, Salt Lake City, UT.

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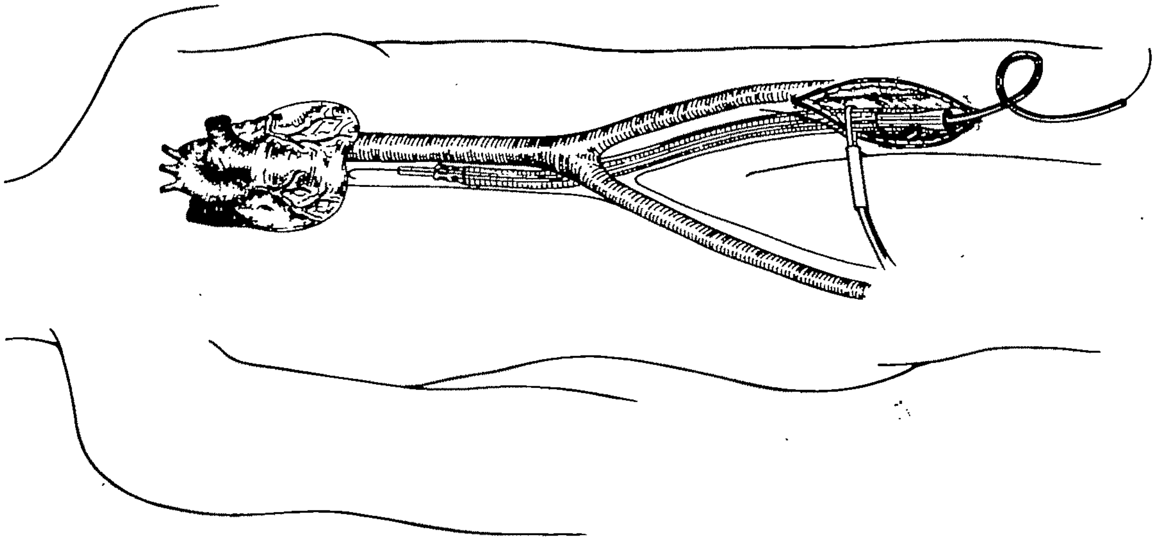

Fig 2. The venous cannula is advanced into the inferior vena cava over the catheter-wire assembly.

Results

We have applied this femoral venous cannulation technique in 5 patients. In all patients the diameter of the femoral vein at the insertion site determined the size of venous cannula inserted. The venous cannulas used ranged in size from 32F to 36F. Cardiopulmonary bypass flows adequate to perform the planned procedures were achieved in 4 of the 5 patients. In the fifth patient, the need to use profoundly hypothermic circulatory arrest to repair an aortic arch injury required additional cannulation of the pulmonary artery for adequate cardiac decompression. In no patient were there any complications related to femoral venous cannulation.

Comment

Increasing use of femorofemoral cardiopulmonary bypass in certain situations has emphasized the need to be able to reliably obtain adequate venous drainage in a safe and rapid manner. Patient positioning and local anatomy may make passage of large venous cannulas difficult, if not impossible. In addition, forceful advancement of a rigid cannula into the femoral and iliac veins may lead to disastrous complications such as vessel laceration. We have applied this technique of femoral venous cannulation with uniform success in our small series of patients. Because it is a relatively simple technique that allows for rapid and reliable femoral venous cannulation, we recommend its use.

References

1. Ungerleider RM, Mills NL, Wechsler AS. Left thoracotomy for reoperative coronary artery bypass procedures. Ann Thorac Surg 1985;40:11–5.

Evolution of Therapy for Pharyngoesophageal (Zenker's) Diverticulum

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The early publications of Zenker and later reports by Clagett and Payne highlight our understanding of the pathophysiology and treatment of pharyngoesophageal diverticulum. A historical review of events surrounding these contributions provides perspectives on their respective roles in the development of current therapy for this disorder.

(Ann Thorac Surg 1991;51:848–52)

Pharyngoesophageal diverticula are fascinating problems that continue to challenge surgeons to this day. Although they were first described more than two centuries ago, surgeons have adopted appropriate therapeutic techniques only in the past 30 years. The evolution of therapy for these disorders is an object lesson in the science of surgery, emphasizing the need to understand pathophysiology to ensure successful treatment.

During the mid-eighteenth century, interest in pathological anatomy flourished, perhaps most actively in the practices of the Hunter brothers. The first record of a pharyngoesophageal diverticulum was communicated to William Hunter by Abraham Ludlow in 1764 [1], described as a "preternatural Dilatation of, and Bag formed in, the Pharynx"; the autopsy specimen from the case was registered in the Hunterian Museum (Fig 1). Additional reports of such anomalies were published in Italy and Germany in the latter half of the eighteenth century.

In 1816 Sir Charles Bell published his volume *Surgical Observations* [2], which was only one of a large number of important medical contributions he was to make. Although he worked as a surgeon, he is perhaps best known for his contributions as a neurologist and anatomist, having described the long thoracic nerve (Bell's nerve) and the condition resulting from damage to the facial nerve (Bell's palsy). Until the time of his 1816 publication, pharyngoesophageal diverticula were thought to be congenital or of traumatic origin. Bell was the first to define the two abnormal components necessary for their development: discoordination between the inferior pharyngeal constrictors and the cricopharyngeus muscle, and a preexisting anatomical defect between these muscles. His prescient observations regarding the pathophysiology of pharyngoesophageal diverticula predated our current understanding of this condition by nearly 100 years.

In 1840 Rokitansky [3] first described traction diverticula of the thoracic esophagus. He was also aware of pharyngoesophageal diverticula, but inaccurately believed these to result from pressure by ingested food or distal obstruction secondary to stricture or extrinsic compression. During the middle of the nineteenth century there was considerable confusion regarding the etiology and appropriate terminology for the variety of diverticula affecting the esophagus. This confusion was largely resolved by Albert Frederich Zenker.

Born in 1825, Zenker was educated in Leipzig and received his medical doctorate in 1851. He was primarily a pathologist, and he served in that capacity as Professor in both Leipzig (1855) and Erlangen (1862). Perhaps his most outstanding work was on the normal and pathological anatomy of the lung, resulting in a treatise published in Dresden in 1862 containing the first description of a pulmonary fat embolism. He is also credited with coining the terms *pneumoconiosis* and *anthracosis*. In 1877, with von Zeimssen, Professor in Munich, he published "Krankheiten des Oesophagus" [4], the best compendium of information on esophageal ulceration and diverticula in the second half of the nineteenth century. This work contains many items of general interest on the esophagus, including disease etiology, symptoms, diagnosis, and general therapy. There are major sections on stricture, diverticula, rupture and perforation, esophagitis, and hemorrhage.

In this article Zenker and von Zeimssen describe for the first time the separation of diverticula into two etiologic categories: traction and pulsion. Traction diverticula, as first described by Rokitansky, were believed to develop as a result of forces exerted from the outside, due to inflammatory adhesions caused by infections of the vertebral bodies or tuberculous bronchial lymph nodes. In contrast, pulsion diverticula, they proposed, developed as a result of forces from within the esophageal muscular tube acting against an area of resistance. They summarized 23 previously published cases, adding 5 of their own, in a very detailed description of the clinical findings and gross anatomy of this disorder (Fig 2).

These concepts regarding the etiology of various esophageal diverticula were quickly accepted, although confusion persisted as to the anatomical location and appropriate nomenclature for the disorders. Many authors continued to refer to the pharyngoesophageal diverticula incorrectly as esophageal diverticula, believing they originated through the muscular wall of the esophagus. In 1908 Killian [5] clarified the anatomical site of origin as the space between the inferior pharyngeal constrictor muscles

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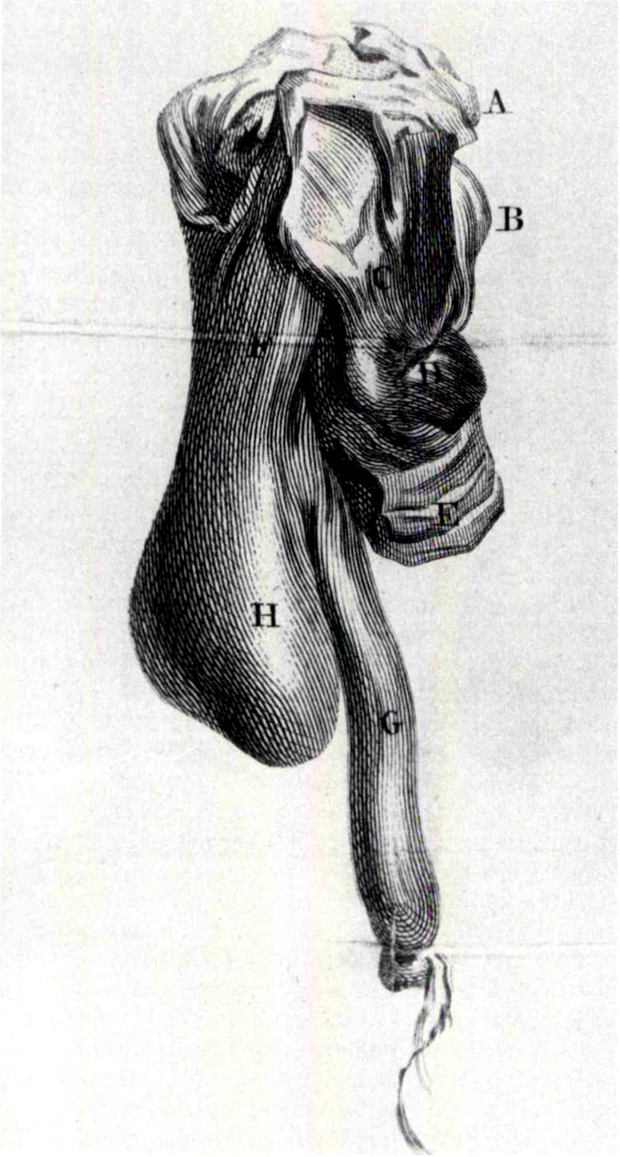

Fig 1. A drawing of the first case of pharyngoesophageal diverticulum from the autopsy performed by Ludlow as reported to William Hunter in 1764. (Reprinted from Ludlow A. A case of obstructed deglutition, from a preternatural dilatation of, and bag formed in, the pharynx. Med Observations and Inquiries 1767;3:85. From the Rare Books Collection, The Crerar Library, The University of Chicago.)

and the cricopharyngeus muscle, in contrast to the triangle of Laimer, initially thought to be the site of origin, which is located more laterally and inferiorly. Finally, an important article by Bensaude, Gregoire, and Guenaux in 1922 [6] provided the definitive classification for diverticula according to location and cause. Pulsion diverticula in the cervical region originated at or below the inferior pharyngeal constrictor muscles and were termed *pharyngoesophageal diverticula*; other pulsion diverticula were found just above the level of the diaphragm, so called *epiphrenic diverticula*; and traction diverticula were found primarily in the peribronchial region.

Initial Therapeutic Efforts

Preliminary thoughts on managing pharyngoesophageal diverticula originated as early as 1830, when Bell [7] proposed the establishment of a fistula to empty the diverticulum of its contents. The first recorded practice of this was by Nicoladoni in Vienna in 1877 [8]. An unsuccessful attempt at excision of the diverticulum, first suggested by Kluge in 1850 [9], was performed in 1884 by Niehans [10]. The first successful resection was by

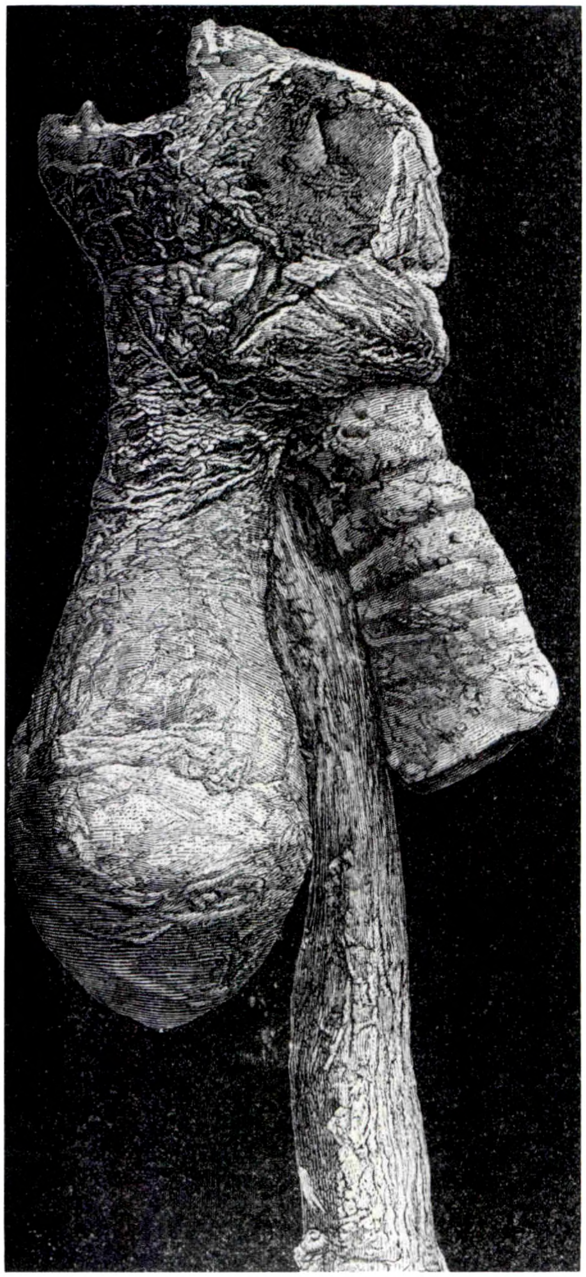

Fig 2. An illustration of a pulsion diverticulum of the pharynx included in Zenker's landmark paper. (Reprinted from Zenker FA, von Ziemssen H. Krankheiten des Oesophagus. In: von Ziemssen H, ed. Handbuch der Speciellen Pathologie und Therapie, vol 7 (Suppl). Leipzig, FC Vogel, 1877.)

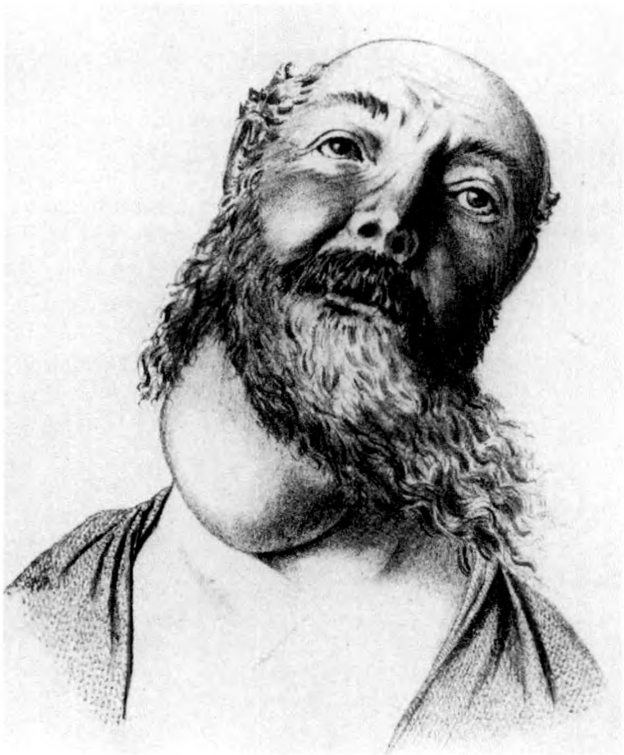

Fig 3. The preoperative appearance of Captain E. before undergoing the first successful resection of a pharyngoesophageal diverticulum by Wheeler in 1885. (Reprinted from Wheeler WI. Pharyngocoele and dilatation of pharynx, with existing diverticulum at lower portion of pharynx lying posterior to the oesophagus, cured by pharyngotomy, being the first case of the kind recorded. Dublin J Med Sci 1886;82: 349–57.)

Wheeler in 1885 (Fig 3) [11], followed by additional favorable reports of von Bergmann and Kocher in 1892 [12, 13] and Butlin and Billroth in 1893 [14, 15]. Diverticulectomy was not the only operation attempted for this disorder, however. In 1896 Girard [16] devised a method of invaginating the diverticulum into the esophagus, oversewing the resultant dimple. In some cases this procedure led to very satisfactory results, although at least one complete recurrence was documented by Waggett and Davis [17] in a patient after a fit of violent sneezing. Diverticulopexy was also described in this early period by Schmid [18], and was first performed by Hill in 1917 [19].

The accurate recognition of and subsequent therapy for pharyngoesophageal diverticula was sufficiently well known by 1910 that Stetton was able to publish a list of all cases operated on up to that time organized according to surgical technique [20]. These methods included primary excision, excision after preliminary gastrostomy, invagination of the sac, mucosal destruction without excision, and two-stage excision. The series totalled 60 patients, of whom 10 died, for an operative mortality of "only 16.6%." In patients surviving these efforts, primary healing occurred in only 42%. The two-stage operation was devised to avoid the catastrophic complications of an uncontrolled pharyngocutaneous salivary fistula, the primary cause of morbidity and mortality after these early resections. It was first proposed by Goldmann, who reported a successful case in 1909 [21]. Additional reports of its use quickly followed, including that of C. H. Mayo in 1910 [22]. The original description consisted of ligation of the neck of the sac and implantation of the sac in the wound, to be removed at a second stage 2 weeks later after its sloughing. Modifications of this technique included, among others, suturing of the sac to the wound without ligating the neck as a first stage [23] and separation of the mucosa from the submucosa at the second stage, leaving the submucosa in the wound after excision of the mucosal sac to allow a more controlled salivary fistula [24].

One-Stage Versus Two-Stage Technique

Fear of an uncontrolled pharyngocutaneous salivary fistula, the primary cause of death after treatment of a pharyngoesophageal diverticulum, was prominent in the early decades of the twentieth century. This concern was reflected in the triumphant title of an article by Mixter, which summarized the contents of his paper in an unusually complete manner [25]. Despite early satisfactory experience with the one-stage technique, C. H. Mayo used the two-stage technique commonly through the 1920s, reporting on 74 operations with only three deaths in 1923 [23]. This technique was modified by Lahey, who championed its use through the 1940s, publishing at least 19 articles on it during that period [26, 27]. The one-stage technique also yielded good results in this early era: Lupke reported 39 cases with two deaths in 1921 [28], and Shallow recorded 76 patients with two deaths in 1936 [29]. The transition from the more popular two-stage operation to the one-stage operation was a fitful one during the 1930s and 1940s. Harrington reported a series of 33 cases in 1937, 25 completed by the two-stage operation [30], whereas after that report he performed an additional 107 cases, all by the one-stage technique [31]. It is a commentary on the heated debate stemming from this controversy that proponents of the two different operations, Lahey at his clinic and Harrington at the Mayo Clinic, rarely referred to each other's work.

By the 1950s almost all operative therapy for pharyngoesophageal diverticula employed the one-stage technique, primary excision and closure, although an agonal reference to the two-stage technique by Lahey and Warren appeared in 1954 [32]. The quintessential paper on the use of the one-stage technique was published in 1960 by Clagett and Payne, both of the Mayo Clinic, in which they summarized results in 478 patients treated from 1944 through 1957 [33]. The article is a model of breviloquent writing, describing the mode of presentation, operative indications, and results in only five pages of text. The technique is carefully explained: ". . . a curved clamp is placed over the neck of the sac in a transverse position. . . . the mucosa is excised in stages proximal to the clamp. Interrupted silk sutures are used to close the mucosa as it is cut. . . . When the diverticulum is completely excised and the mucosa closed, the muscular and fascial layers of the hypopharynx are closed in a transverse plane with fine continuous catgut sutures."

What is missing from this treatise is information on long-term results of the operation. Clagett and Payne state that information was available for only about half of the patients. Of these, recurrence of the diverticulum was found in 2.5%, and 4.1% had postoperative dysphagia of a serious degree. Thus, almost 7% of those followed up had unsatisfactory results after excision of the diverticulum alone in a single stage.

Modern Therapy

Although largely successful, techniques for managing pharyngoesophageal diverticula that relied primarily on diverticulectomy ignored the underlying pathophysiology of this disorder. Sir Charles Bell suggested the discoordinate activities of the inferior pharyngeal constrictor pushing against a closed cricopharyngeus muscle as the cause for such diverticula. This mechanism was rediscovered by Killian in 1907 [34] and affirmed by Jackson and Shallow in 1926 [35]. The first cricopharyngeal myotomy was inadvertently performed by Richardson in 1899 [36] during digital dilation of a high esophageal stricture after diverticulectomy. This was repaired by esophagoplasty with good long-term results. Subsequent efforts to endoscopically divide the cricopharyngeus muscle by cutting the septum at the base of the diverticulum were met with tragic consequences due to the development of mediastinitis and bleeding [37]. This technique was revived with some success by Dohlman and Mattsson decades later [38]. Dilation of the cricopharyngeus muscle was advised as being vital to operation for pharyngoesophageal diverticula by many authors [39, 40].

Perhaps the introduction of the term *cricopharyngeal achalasia*, proposed by Asherson in 1950 [41], stimulated the development of current techniques of myotomy for management of these problems. Kaplan reported the first intentional external cricopharyngeal myotomy in 1951 [42]. This success stimulated the use of myotomy for amyotrophic lateral sclerosis, cervical dysphagia secondary to gastroesophageal reflux, and during reconstruction after resection of the base of the tongue, epiglottis, or pharynx for cancer. Not surprisingly, the operation was also quickly applied as a primary mode of treatment for cricopharyngeal diverticula by a number of surgeons.

The first report of external division of the cricopharyngeus for pharyngoesophageal diverticula was by Harrison in 1958 [43], who recorded 8 cases treated by this technique, 2 managed by dilation alone, and 17 managed by endoscopic division of the septum. This was followed closely by carefully conducted manometric investigations of pharyngeal and cricopharyngeal activity associated with such diverticula [44], which conclusively documented instances of discoordination previously suggested by radiographic and endoscopic observations. Several authors suggested that addition of a myotomy to primary excision might prevent recurrence of the diverticulum [44–47]. The landmark reports by Belsey [48] and Ellis and co-workers [49] firmly established the role of myotomy for this disorder by summarizing excellent results in large series of 29 and 18 patients, respectively. Recent data [50] confirm the reliability of this approach and support the continued use of diverticulum suspension rather than excision, first proposed by Schmid and popularized by Belsey.

These recent data underscore the presence of demonstrable cricopharyngeal dysfunction in the majority of patients with pharyngoesophageal diverticula. The small percentage of patients with apparently normal function emphasizes our failure to completely understand the underlying pathophysiological mechanisms in every individual. Nevertheless, the evolution of the therapeutic approach to such disorders to correctly include cricopharyngeal myotomy represents the successful culmination of nearly two centuries of observation and speculation.

References

1. Ludlow A. A case of obstructed deglutition, from a preternatural dilatation of, and bag formed in, the pharynx. Med Observations and Inquiries 1767;3:85–101.
2. Bell C. Surgical observations. London: Longmans, Greene and Co, 1816:64–70.
3. Rokitansky C. Divertikel am Pharynx. Jahrb Dkk Osterr Staates 1840;30:222–5.
4. Zenker FA, von Ziemssen H. Krankheiten des Oesophagus. In: von Ziemssen H, ed. Handbuch der Speciellen Pathologie und Therapie, vol 7 (suppl). Leipzig: FC Vogel, 1877:1–87.
5. Killian G. La boudre de l'oesophage. Ann Mal Orielle Larynx 1908;34:1.
6. Bensaude R, Gregoire R, Guenaux G. Diagnostic et traitement des diverticules oesophagiens. Arch Mal App Digest 1922;12:145–203.
7. Bell C. Cited by Bensaude R, Gregoire R, Guenaux G. Diagnostic et traitement des diverticules oesophagiens. Arch Mal App Digest 1922;12:145–203.
8. Nicoladoni K. Behandlung der Oesophagusdivertikel. Wien Med Wochenschr 1877;25:606–607.
9. Kluge. Cited by Konig F. Die Krankheiten des unteren Theiles des Pharynx und des Oesophagus. Deutsche Chir 1880;35:94.
10. Niehans. Cited by Girard C. Du traitement des diverticules de l'oesophage. Congres Franc Chir 1896;10:392–407.
11. Wheeler WI. Pharyngocele and dilatation of pharynx, with existing diverticulum at lower portion of pharynx lying posterior to the oesophagus, cured by pharyngotomy, being the first case of the kind recorded. Dublin J Med Sci 1886;82: 349–57.
12. Von Bergmann E. Ueber den Oesophagusdivertikel und seine Behandlung. Arch Klin Chir 1892;43:1–30.
13. Kocher T. Das Oesophagusdivertikel und dessen Behandlung. Correspondblatt Schweiz Aerzte 1892;22:233–44.
14. Butlin HF. On the removal of a pressure pouch of the oesophagus. Med Chir Trans 1893;76:269–78.
15. Schwarzenbach E. Zur operativen Behandlung und Aetiologie der Oesophagusdivertikel. Wien Klin Wochenschr 1893; 6:435–40, 453–5, 474–6.
16. Girard C. Du traitement des diverticules de l'oesophage. Congres Franc Chir 1896;10:392–407.
17. Waggett EB, Davis ED. A case of pharyngeal diverticulum. Lancet 1912;1:786.
18. Schmid HH. Vorschlag eines einfachen Operationsverfahr-

ens zur Behandlung des Oesophagesdivertikels. Wien Klin Wochenschr 1912;25:487–8.

19. Hill W. Pharyngeal pouch treated by diverticulopexy. Proc R Soc Med 1917–1918;11:60.
20. Stetten D. The radical extirpation of pharyngo-oesophageal pressure diverticula. Ann Surg 1910;51:300–19.
21. Goldmann EE. Die zweizeitige Operation von Pulsiondivertikeln der Speiseröhre. Beitr Klin Chir 1909;61:741–9.
22. Mayo CH. Diagnosis and surgical treatment of oesophageal diverticula. Ann Surg 1910;51:812–7.
23. Mayo CH. Treatment of diverticula of the esophagus. Ann Surg 1923;77:267–71.
24. Lahey FH. The technique of the two stage operation for pulsion oesophageal diverticulum. Surg Gynecol Obstet 1926;43:359–65.
25. Mixter SF. Congenital oesophageal pouch: excision; immediate suture of oesophagus; recovery. Trans Am Surg Assoc 1895;8:357–60.
26. Lahey FH. Oesophageal diverticula. Boston Med Surg J 1923;188:355–62.
27. Lahey FH, Hoover WB. Pharyngoesophageal diverticulum. N Engl J Med 1937;216:591–7.
28. Lupke H. Beitrage zur operativen Behandlung der Oesophagusdivertikel. Bruns Beitr Klin Chir 1921;121:612–28.
29. Shallow TA. Combined one stage closed method for the treatment of pharyngeal diverticula. Surg Gynecol Obstet 1936;62:624–33.
30. Harrington SW. Pulsion diverticula of the hypopharynx. Surg Gynecol Obstet 1939;69:364–73.
31. Harrington SW. Pulsion diverticulum of the hypopharynx at the pharyngo-esophageal junction. Surgery 1945;18:66–81.
32. Lahey FH, Warren KW. Esophageal diverticula. Surg Gynecol Obstet 1954;98:1–28.
33. Clagett OT, Payne WS. Surgical treatment of pulsion diverticula of the hypopharynx: one-stage resection in 478 cases. Dis Chest 1960;37:257–61.
34. Killian G. The mouth of the esophagus. Laryngoscope 1907;17:421–8.
35. Jackson C, Shallow TA. Diverticula of the oesophagus, pulsion, traction, malignant and congenital. Ann Surg 1926;83:1–19.
36. Richardson MH. Two cases of oesophageal diverticulum, with remarks. Ann Surg 1900;31:525–46.
37. Mosher HP. Webs and pouches of the oesophagus, their diagnosis and treatment. Surg Gynecol Obstet 1917;25:175–87.
38. Dohlman G, Mattsson O. The endoscopic operation for hypopharyngeal diverticula. Arch Otolaryngol 1960;71:744–52.
39. Negus VE. The etiology of pharyngeal diverticula. Bull J Hopkins Hosp 1957;101:209–23.
40. Korkis FB. The aetiology, diagnosis and surgical treatment of pharyngeal diverticula. J Laryngol Otol 1958;72:509–22.
41. Asherson N. Achalasia of the cricopharyngeal sphincter. J Laryngol Otol 1950;64:747–58.
42. Kaplan S. Paralysis of deglutition: a post poliomyelitis complication treated by section of the cricopharyngeus muscle. Ann Surg 1951;133:572–6.
43. Harrison MS. The aetiology, diagnosis and surgical treatment of pharyngeal diverticula. J Laryngol Otol 1958;72:523–34.
44. Cross FS, Johnson GF, Gerein AN. Esophageal diverticula. Arch Surg 1961;83:525–33.
45. Lewis RS, Edwards WG. The treatment of pharyngeal diverticula. Br J Surg 1962;50:1–5.
46. Wilkins SA Jr. Indications for section of the cricopharyngeus muscle. Am J Surg 1964;108:533–8.
47. Kinley CE. The management of hypopharyngeal diverticulum. Can J Surg 1966;9:27–32.
48. Belsey R. Functional disease of the esophagus. J Thorac Cardiovasc Surg 1966;52:164–88.
49. Ellis FH Jr, Schlegel JF, Lynch VP, Payne WS. Cricopharyngeal myotomy for pharyngo-esophageal diverticulum. Ann Surg 1969;170:340–50.
50. Skinner DB, Altorki N, Ferguson M, Little AG. Zenker's diverticulum: clinical features and surgical management. Dis Esoph 1988;1:19–22.

Prolonged Preservation of Canine Lung Allografts: The Role of Prostaglandins

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The role of prostaglandin E_1 (PgE_1) and prostacyclin in enhancing the ischemic tolerance of single-lung grafts was investigated. Fifteen donor dogs underwent pulmonary artery flushing with 60 mL/kg of 4°C modified Euro-Collins solution; 5 dogs each received a 15-minute infusion of PgE_1, prostacyclin, or saline solution before flushing. After 12 hours of storage at 4°C, left lung transplantation was performed in 15 recipient dogs. Measurements were performed after 10 minutes of right pulmonary artery snaring before transplantation, after transplantation, and after 2, 4, and 6 hours of reperfusion. At 6 hours, the oxygen tensions (on 100% O_2) were 478 ± 64, 296 ± 75, 79 ± 12, and 71 ± 23 mm Hg in control (nontransplanted), prostacyclin-, PgE_1-, and saline-treated dogs, respectively ($p < 0.05$; prostacyclin or control versus saline and PgE_1 dogs). Mean pulmonary artery pressures increased within each group during reperfusion, but were not significantly different among groups. Similarly, peak inspiratory pressures and wet weight to dry weight ratios were not significantly different among groups after 6 hours of reperfusion. We conclude that donor pretreatment with prostacyclin is associated with superior oxygen transfer in canine lung allografts after 12 hours of cold storage, transplantation, and 6 hours of reperfusion. In this model, donor pretreatment with PgE_1 conferred no benefit to prolonged lung allograft preservation.

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Although the prolonged preservation of lung allografts has long been an elusive goal [1], satisfactory 12-hour preservation of single-lung [2] and double-lung [3] grafts is increasingly being achieved experimentally. The challenge for the future is to translate these advances in the experimental laboratory into clinical reality so that the procurement of lung grafts from extended distances will become commonplace.

Prostaglandins are products of arachidonic acid metabolism [4] that have a wide variety of biological effects that may prove beneficial in lung transplantation. In particular, prostaglandin E_1 (PgE_1) and prostacyclin are potent pulmonary vasodilators [4, 5], induce bronchodilatation [4], and have a wide variety of pulmonary protective effects under conditions of chronic hypoxia [6], normothermic ischemia [7, 8], and cardiopulmonary bypass [9], and during isolated heart-lung autoperfusion [10–13]. They also favorably modulate white cell and platelet function by attenuating polymorphonucleocyte sequestration in damaged tissues [8, 14], inhibiting platelet aggregation [4, 15], and preventing lysosomal enzyme release and superoxide anion production by neutrophils in vitro [16]. Furthermore, prostaglandins suppress the vascular permeability that is induced by vasoactive mediators [17] and have a pronounced, but incompletely understood, cytoprotective effect [15].

Either PgE_1 [18–24] or prostacyclin [25–28] is currently employed during organ procurement by many centers There has also been a plethora of experimental studies examining the roles of prostacyclin [9–34] and PgE_1 [35–40] in lung allograft preservation, but only a few of these have compared the function of prostaglandin-treated donor organs with that of allografts procured by the same technique but without the infusion of prostaglandin [30, 32–35]. Furthermore, a recent study has suggested that donor treatment with PgE_1 before 12-hour double-lung preservation and transplantation in dogs was deleterious to immediate graft function [41, 42]. An additional report has found that Iloprost, a stable prostacyclin analogue, administered to the donor before 6-hour canine single-lung preservation conferred no benefit [33]. The present study was therefore performed to ascertain and contrast the pulmonary protective effects of PgE_1 and prostacyclin in extended (12-hour) single-lung preservation and transplantation.

Material and Methods

Thirty size-matched mongrel dogs were randomly allocated to one of three experimental groups, and 5 additional dogs were assigned to a control group. Donor animals were pretreated with methylprednisolone, 250 mg [3, 31, 33], and all animals were premedicated with xylazine, 1 mg/kg, and atropine, 0.04 mg/kg. Anesthesia was induced with thiopental sodium, 12 mg/kg, and maintained with 1% halothane. Neuromuscular blockade was achieved with pancuronium, 0.1 mg/kg, which was

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repeated at intervals. After intubation with a cuffed endotracheal tube, mechanical ventilation was commenced at a tidal volume of 20 mL/kg, at a fraction of inspired oxygen (FiO_2) of 0.5 for the lung donors and 1.0 for the single-lung recipients and the control dogs. All animals received humane care in accordance with the "Principles of Laboratory Animal Care" (National Society for Medical Research), the "Guide for the Care and Use of Laboratory Animals" (National Institutes of Health publication No. 85-23, revised 1985), and the specifications of the Council on Animal Care of the University of Western Ontario.

Donor Operation

After median sternotomy and anterior pericardiectomy, the superior and inferior venae cavae, ascending aorta, pulmonary artery (PA), and trachea were mobilized. The proximal main PA was encircled with a heavy silk tie, which was subsequently snared (proximal to the flush cannula) at the time of infusion of the pulmonary flush solution. A needle thermistor probe was inserted into the depths of the right middle lobe for the measurement of lung temperature during and after flushing. An 18-gauge catheter was introduced into the femoral artery as well as into the distal main PA, and pressures were recorded throughout the lung procurement procedure using a Statham Spectramed P10 EZ pressure transducer (Statham, Oxnard, CA), which was coupled to a Gould TA 2000 chart recorder and monitor (Gould, Cleveland, OH). An additional catheter was placed through a 4-0 polypropylene pursestring suture in the right atrium for the infusion of sterile saline solution, PgE_1, or prostacyclin into the 5 donor dogs in each group.

Heparin, 300 units/kg, was then administered, and a 15-minute infusion of saline solution, PgE_1, or prostacyclin commenced. The PgE_1 (Prostin VR, Upjohn Company of Canada, Don Mills, Ont, Canada) was prepared by diluting 1 mL (0.5 mg) in 100 mL of sterile 5% dextrose. The prostacyclin (Burroughs Wellcome Inc, Kirkland, Que, Canada) was prepared by reconstituting 1 vial (0.5 mg) in its sterile glycine buffer immediately before use and then diluting the mixture in 100 mL of sterile 5% dextrose. Both the PgE_1 and prostacyclin infusions were begun at $0.1\ \mu g \cdot kg^{-1} \cdot min^{-1}$, and the dose of each was readjusted to maintain a steady-state infusion that reduced the systolic arterial pressure by 40%.

After 15 minutes, a No. 14 Bard cannula was inserted into the proximal main PA and secured. The PgE_1 and prostacyclin infusions were continued during PA cannulation and during the subsequent flush. After inflow occlusion, the tip of the left atrial appendage was amputated and the PA was flushed with 60 mL/kg of 4°C Euro-Collins solution [43, 44], which had been modified by the addition of 8 mEq of magnesium sulfate and 65 mL of 50% dextrose/L [20, 21, 36, 37]. The pulmonary flush solution was given by gravity drainage, and the PA pressure was monitored as well as the duration of the infusion so that pulmonary vascular resistance during the flush (pulmonary flush resistance) could be calculated [45, 46]: pulmonary flush resistance ($mm\ Hg \cdot mL^{-1} \cdot s^{-1}$) = (mean pulmonary flush pressure)/[(flush volume)/(flush time)]. Additional topical cooling was provided by 4°C sterile saline solution, which was allowed to collect in the pleural cavities during excision of the heart and lungs.

After completion of the pulmonary flush, the heart was excised. Mechanical ventilation was continued during the infusion of pulmonary flush solution and during the cardiectomy, and the trachea was then clamped at end-inspiration and divided. The double-lung block was then removed, and care was taken to minimize handling of the lungs. The lungs were placed in a basin containing cold, sterile saline solution, and the right lung was excised, leaving generous cuffs of left main bronchus, left PA, and left atrium surrounding the left pulmonary veins. The left main bronchus was clamped, and the left lung was placed in a plastic bag containing sterile saline solution. It was then transferred to a water cooler and stored at 4°C for 12 hours.

Recipient Operation

On the next day a weight-matched recipient dog (15 to 30 kg) was anesthetized as described in the preceding section. A posterolateral thoracotomy was performed through the fifth intercostal space, and the pericardium was opened anteriorly and posteriorly to the phrenic nerve. The right and left PAs were encircled with heavy silk ties for subsequent snaring during hemodynamic and blood gas measurements. Femoral artery and main PA catheters were inserted as during the donor procedure. The left chest was then closed using towel clips, leaving a 2-cm opening on the anterior aspect of the thoracotomy incision through which the PA snares could be manipulated. The animal was placed in a supine position, and measurements of PA pressure, arterial blood gases, and peak inspiratory pressure [31, 33] were recorded at an FiO_2 of 1.0. The left PA was then snared, and blood gas, hemodynamic, and peak inspiratory pressure determinations were repeated after 10 minutes of occlusion [2, 47]. The snare was released, and both lungs were perfused for an additional 10 minutes. The right PA was then occluded for 10 minutes and hemodynamic, blood gas, and peak inspiratory pressure determinations were repeated.

The right PA snare was released, the chest was reopened, and a left pneumonectomy was performed, preserving generous stumps of left PA and left main bronchus. A clamp was applied intrapericardially on the left atrium, and the pulmonary veins were joined to create a single left atrial cuff. The donor lung was then removed from its 4°C bath and was covered with a moist gauze sponge. The left lung transplantation was performed using two 5-0 polypropylene horizontal mattress sutures for the left atrial anastomosis, a single running 5-0 polydioxanone suture for the left main bronchial anastomosis, and two 6-0 polypropylene sutures for the PA anastomosis. Before the PA suture was tied, the bronchial clamp was released, and the transplanted lung was reinflated. The atrial clamp was then released, and after backbleeding appeared at the PA anastomosis, the PA clamp was released and the suture secured. The chest was then closed, as previously, and the dog was transferred to the supine position.

Table 1. Comparison of Donor and Recipient Weights and Ischemic Times Among Experimental Groups[a]

	Experimental Group		
Variable	PgE_1	Prostacyclin	Saline
Donor weight (kg)	20 ± 1.5	20 ± 1.9	19 ± 0.6
Recipient weight (kg)	23 ± 2	19 ± 1	19 ± 1.7
Warm ischemic time (min)	44 ± 2	43 ± 4	49 ± 3
Cold ischemic time (h)	12.3 ± 0.3	12.1 ± 0.2	12.2 ± 0.1
Total ischemic time (h)	13.0 ± 0.3	12.8 ± 0.2	13.0 ± 0.1

[a] Values are expressed as mean ± standard error of the mean. $p > 0.05$ among all variables on each line.

PgE_1 = prostaglandin E_1.

Hemodynamic, blood gas, and peak inspiratory pressure measurements were repeated using the same sequence of PA occlusion as noted previously [2, 47]. The recipient animals were monitored for an additional 6 hours postoperatively, and all measurements were repeated at 2, 4, and 6 hours with the animals in the supine position and ventilated at an FiO_2 of 1.0. The dogs were then killed, the anastomoses were inspected, and 3-g specimens of the transplanted left lung as well as the native right lung were excised, blotted dry, and weighed on a Mettler analytical balance. The lung specimens were desiccated in an 80°C oven for 48 hours and reweighed for the determination of wet weight to dry weight ratios.

Control Animal Operation

The 5 dogs in the control group underwent a left posterolateral thoracotomy, pericardiotomy, and insertion of right and left PA snares as well as femoral artery and main PA catheters for pressure measurements. They were anesthetized in the same manner as the recipient animals and ventilated at an FiO_2 of 1.0, but did not undergo transplantation. Blood gas, hemodynamic, and peak inspiratory pressure measurements were performed under identical conditions and at the same time intervals as in the dogs that received a left lung transplant.

Statistical Analysis

Results were expressed as mean ± the standard error of the mean. The three experimental groups and the control animals were compared using analysis of variance, as computed by the Instat statistical software program (San Diego, CA). In all cases, Bonferroni's correction was used to confirm statistical significance. Comparison of data at different time intervals within each experimental group was performed by the two-tailed t test. Statistical significance was judged to be present if a probability value less than 0.05 was obtained.

Results

There were no significant differences among groups in the weights of the donor and recipient animals or in the warm, cold, and total ischemic times of the lung allografts (Table 1). The control dogs weighed a mean of 21.5 ± 1.5 kg ($p > 0.05$ compared with all of the experimental groups).

The mean dose of prostaglandin required to produce a steady-state decrease in the systolic blood pressure by 40% during the 15-minute infusion in the donor was 0.52 ± 0.14 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in the PgE_1 group and 0.19 ± 0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in the prostacyclin group ($p = 0.05$). The 15-minute infusion of sterile saline solution was associated with no measurable hemodynamic change in donor animals. The pulmonary flush resistance was 1 ± 0.3 $mm\ Hg \cdot mL^{-1} \cdot s^{-1}$ in saline-treated donors, 0.35 ± 0.05 $mm\ Hg \cdot mL^{-1} \cdot s^{-1}$ in donors after PgE_1 infusion, and 0.25 ± 0.04 $mm\ Hg \cdot mL^{-1} \cdot s^{-1}$ in donors after prostacyclin pretreatment ($p < 0.05$, prostacyclin or PgE_1 versus saline; $p = 0.11$, prostacyclin versus PgE_1). Despite the marked decrease in pulmonary flush resistance in the two prostaglandin groups, the temperature registered by the thermistor probe in the right middle lobe was similar in the three groups at the completion of the PA flush (13.6 ± 0.9°, 13.6 ± 2.4°, and 14.2 ± 3.9°C in the PgE_1-, prostacyclin-, and saline-treated donors, respectively; $p > 0.8$).

The changes in oxygen tension (PO_2) of the recipient and control (nontransplanted) animals measured at an FiO_2 of 1.0 after 10 minutes of right PA snaring are illustrated in Figure 1. There were no significant differences in PO_2 among the three experimental and control groups preoperatively. Immediately postoperatively and after 2 hours of reperfusion, all three experimental groups had significantly worse PO_2s than control animals during right PA snaring; there were no significant differences among groups. At 4 hours, the PO_2s in the saline and PgE_1 groups were significantly worse than in control dogs, but the PO_2 of the prostacyclin group was not. After 6 hours of reperfusion, the PO_2 of the prostacyclin-treated lungs (with the right PA snared) was significantly better than that of the PgE_1 and saline groups. The PO_2 of the prostacyclin group at 6 hours was not significantly different from control (nontransplanted) dogs who were ventilated with 100% oxygen for an identical time (296 ± 75 versus 478 ± 64 mm Hg; $p = 0.10$).

The changes in mean PA pressure under baseline conditions and with the right PA snared before and after transplantation are shown in Figure 2. Ten-minute occlusion of the right PA produced similar and significant increases in mean PA pressure under baseline conditions in the control dogs and in animals in all three experimental groups. After left lung transplantation, there were significant increases in mean PA pressure with the right PA snared within each experimental group; these were most pronounced in the saline-treated allografts. There were no significant differences in mean PA pressures, however, that distinguished one experimental group from another or from the control group during reperfusion. Similarly, no significant differences were detected in peak inspiratory pressures with the right PA snared among the three experimental and control groups (Table 2), indicating the relative insensitivity of this index of pulmonary preservation.

The mean wet weight to dry weight ratios of the

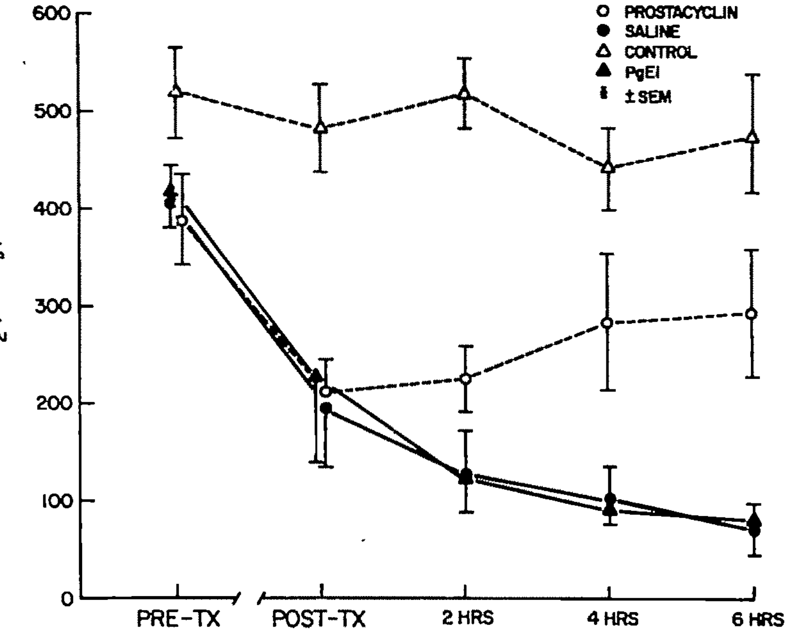

Fig 1. Changes in arterial oxygen tension (PO_2) of recipient and control (nontransplanted) animals measured on 100% O_2 after 10 minutes of right pulmonary artery snaring before and after transplantation. (PgE_1 = prostaglandin E_1; SEM = standard error of the mean.)

transplanted left lungs, nontransplanted right lungs, and control lungs are depicted in Figure 3. The transplanted lungs were significantly more edematous than the nontransplanted lungs within each experimental group, but there were no significant differences in wet weight to dry weight ratios among the three experimental groups after 12 hours of storage and 6 hours of reperfusion.

Comment

Because the delicate alveolar-capillary membrane network of the lungs exhibits a marked sensitivity to ischemia, the long-term preservation of lung allografts has lagged behind the preservation of other organs for transplantation [1]. After more than a quarter century of research, however, satisfactory 12-hour preservation of single-lung [2] and double-lung [3] grafts is attainable in the experimental laboratory. Clinically, lung ischemic times of 4 to 5 hours appear to be well tolerated during long distance procurement [18, 20, 21, 23, 25–27], although recent experience indicates that this ischemic time can be safely extended to more than 6 hours [28].

Although modified Euro-Collins solution has long been the standard pulmonary flush solution for lung preservation both experimentally [30–37, 39, 40, 44, 48] and clinically [19–23, 28], it is well known that PA flushing with cold Euro-Collins solution is associated with increased pulmonary vascular resistance and decreased lung compliance [49]. This fact has provided the impetus for donor treatment with pulmonary vasodilators before cold Euro-Collins flush during lung allograft procurement.

Both PgE_1 and prostacyclin are potent pulmonary vasodilators [4, 5] and have been noted to have beneficial

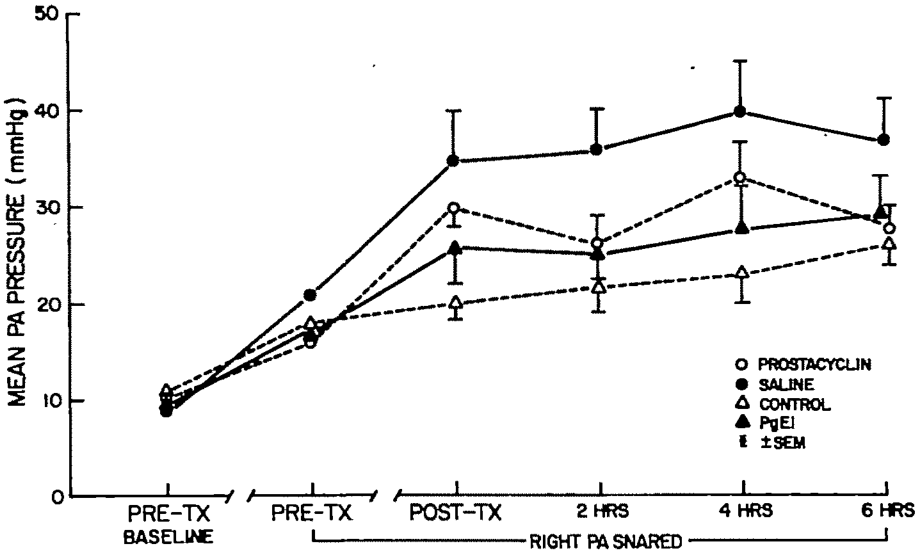

Fig 2. Changes in mean pulmonary artery (PA) pressure of recipient and control (nontransplanted) animals under baseline conditions and with the right pulmonary artery snared before and after transplantation (TX). (PgE_1 = prostaglandin E_1; SEM = standard error of the mean.)

Table 2. Changes in Peak Inspiratory Pressure (cm H_2O) With the Right Pulmonary Artery Snared[a]

Experimental Group	Before Transplantation	Immediately After Transplantation	2 h	4 h	6 h
PgE_1	18 ± 1.2	20 ± 0.5	21 ± 0.9	23 ± 0.8	23 ± 1
Prostacyclin	18 ± 0.8	18 ± 1.2	18 ± 1.3	19 ± 1.2	19 ± 1.5
Saline	20 ± 1.7	22 ± 1.8	22 ± 2	21 ± 1.9	22 ± 3

[a] Values are expressed as mean ± standard error of the mean. $p > 0.05$ among all variables between groups.

PgE_1 = prostaglandin E_1.

effects on the lungs under conditions of chronic hypoxia [6], normothermic ischemia [7, 8], and cardiopulmonary bypass [9], and during heart-lung autoperfusion [10–13]. Despite the widespread use of PgE_1 and prostacyclin in experimental and clinical lung allograft preservation, properly controlled experiments documenting the benefit of prostacyclin and especially PgE_1 are few. In particular, only one study comparing primate lung donors treated with PgE_1 with lung donors that were not treated with PgE_1 has shown improved oxygenation in the early reperfusion phase after 6 hours of ischemia, although the PO_2 at 6 hours of reperfusion was not significantly different between groups [35]. Furthermore, a recent experiment evaluating the role of donor PgE_1 infusion before 12-hour storage and transplantation of canine double-lung grafts found that PgE_1 resulted in decreased oxygenation and an increased alveolar-arterial oxygen gradient after 30 minutes of reperfusion [41, 42]. The only clinical study examining the role of donor treatment with PgE_1 demonstrated a lower peak inspiratory pressure early postoperatively in the PgE_1 group, but no significant difference in alveolar-capillary PO_2, implantation response, and time to extubation between the PgE_1 group and historical controls [19, 24]. The results of our current experiment do not support the concept that donor treatment with PgE_1 is helpful in prolonged lung allograft preservation.

The evidence that prostacyclin is beneficial in lung and heart-lung preservation appears to be more solidly grounded in the literature. After heterotopic heart–left lung transplantation in dogs after 6 hours of ischemia, oxygenation was significantly better in prostacyclin-treated grafts throughout the 12-hour reperfusion phase [32]. The improved function of prostacyclin-treated heart-lung grafts was reaffirmed in a further study by the same group [30], although donor and recipient treatment with oxygen free radical scavengers was found to provide even better lung preservation after 6 hours than Euro-Collins flush with prostacyclin pretreatment. A recent report in a canine model of unilateral lung transplantation confirmed that donor pretreatment with a synthetic prostacyclin analogue (Iloprost) followed by Euro-Collins flush was superior to topical cooling of the lung after complete absorption atelectasis in the donor animals; unfortunately, no control group of Euro-Collins flush without Iloprost pretreatment was used [31]. In a well-controlled experiment of canine single-lung transplantation after modified Euro-Collins flush, an infusion of Iloprost in donors resulted in a significant improvement of PO_2, alveolar-arterial O_2 difference, and PA pressure after 4 hours of ischemia and 1 hour of reperfusion [34]. This occurred despite the fact that lung temperatures were not significantly different between the Iloprost and non-Iloprost groups during and after the administration of the Euro-Collins flush. In addition, the PO_2, alveolar-arterial O_2 difference, and mean PA pressure were not significantly different between 4 and 24 hours of reperfusion [34].

To our knowledge there has been only one study in the English-language literature that concludes that Iloprost treatment of the donor before lung storage and transplantation confers no benefit [33]. In that experiment, a low dose of Iloprost was employed (20 $ng \cdot kg^{-1} \cdot min^{-1}$ as opposed to 190 ± 30 $ng \cdot kg^{-1} \cdot min^{-1}$ of prostacyclin in the current study), and the lungs were stored at 4°C for 6 hours before left lung transplantation and contralateral PA ligation. Only 20 mL/kg of modified Euro-Collins solution was used as a flush in an attempt to highlight the contribution of Iloprost to lung allograft preservation. The addition of Iloprost produced no demonstrable benefit in terms of lung cooling and perfusate distribution during procurement or in the postoperative function of the transplanted lung as measured by PO_2, pulmonary vascular resistance, and peak inspiratory pressure [33]. Hooper and associates speculated that a 6-hour storage period may have been insufficient to detect a marginal benefit, or that concomitant steroid therapy of the donor may have masked a beneficial effect of Iloprost.

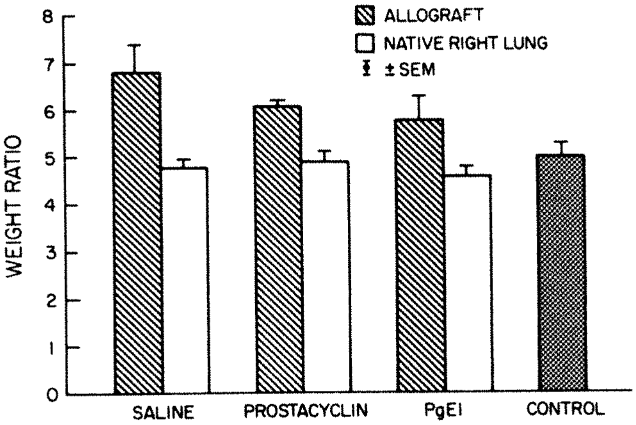

Fig 3. Wet weight to dry weight ratios of the transplanted left lungs and native right lungs of the three experimental groups, and of the left lung in the control (nontransplanted) group. (PgE_1 = prostaglandin E_1; SEM = standard error of the mean.)

The results of our experiment indicate that prostacyclin administration to the donor before prolonged lung allograft preservation is helpful. It is known that the PO_2 is the most sensitive indicator of the status of lung preservation, whereas measurements of pulmonary artery pressure, peak inspiratory pressure, and wet weight to dry weight ratios are less precise [1, 2, 30, 31]. We chose a relatively long ischemic interval and decided to ventilate the recipients with 100% O_2 to determine whether there is a beneficial effect from prostaglandin pretreatment in a "worst-case scenario." It is well documented that continuous ventilation with a high FiO_2 is deleterious in that oxygen-derived metabolites appear to play an important role in the pathogenesis of acute lung injury [50–52]. Nevertheless, the use of 100% oxygen for blood gas and hemodynamic measurements during contralateral PA snaring in the recipients of experimental single-lung grafts is an accepted technique [2, 47]. Furthermore, the ventilation of the control (nontransplanted) animals in our experiment with 100% oxygen for the same duration as animals in the three experimental groups was not associated with a significant decrease in PO_2 of the left lung (522 ± 46 mm Hg at the beginning of the experiment versus 478 ± 64 mm Hg at the end; $p = 0.59$).

The inability of PgE_1 treatment of the donor to provide any benefit in 12-hour lung preservation in this and other recent studies [41, 42] is noteworthy. Although both PgE_1 and prostacyclin significantly reduced pulmonary vascular resistance during flushing with modified Euro-Collins solution in our experiment, no significant differences in lung temperature were noted among the three experimental groups at the termination of the flush. Furthermore, the pulmonary flush resistance was not significantly different in the PgE_1 and prostacyclin donors. The beneficial effect of prostacyclin, as opposed to PgE_1, must therefore be due to properties other than its pulmonary vasodilator effect. The lungs are the major metabolic site for the synthesis, release, and degradation of most prostaglandins, including PgE_1 [4, 53, 54]. Prostacyclin, however, is not inactivated in the lung [5, 53] but is nonenzymatically hydrolyzed to a more stable metabolite in the liver. Furthermore, prostacyclin is at least 30 times more potent than PgE_1 in inhibiting platelet aggregation [4, 55]. Because platelet and leukocyte aggregation in the lungs is a prelude to lung damage after prolonged ischemia and reperfusion, the marked platelet inhibitory effect of prostacyclin and its lack of pulmonary metabolism may be important factors contributing to its superiority to PgE_1 in lung allograft preservation.

In summary, the use of a prostacyclin infusion in the donor before PA flushing and 12-hour cold storage has resulted in significantly improved oxygenation of single-lung allografts. Prostaglandin E_1 employed in a similar manner had no beneficial effect. Further work needs to be done concerning the heterogeneous pulmonary protective effects of these two prostaglandins, and concerning the beneficial properties of prostacyclin, independent of its potent pulmonary vasodilator effect, in experimental and clinical lung transplantation.

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References

1. Haverich A, Scott WC, Jamieson SW. Twenty years of lung preservation—a review. J Heart Transplant 1985;4:234–40.
2. Keshavjee SH, Yamazaki F, Cardoso PF, McRitchie DI, Patterson GA, Cooper JD. A method for safe 12-hour pulmonary preservation. J Thorac Cardiovasc Surg 1989;98:529–34.
3. Bonser RS, Fragomeni LS, Harris K, et al. Acute physiologic changes after extended pulmonary preservation. J Heart Transplant 1990;9:220–9.
4. Moncada S, Flower RJ, Vane JR. Prostaglandins, prostacyclin, thromboxane A_2 and leukotrienes. In: Gilman AG, Goodman LS, Rall TW, Murad F, eds. The pharmacological basis of therapeutics. New York: MacMillan, 1985:660–73.
5. Kadowitz PJ, Chapnick BM, Feigen LP, Hyman AL, Nelson PK, Spannhake EW. Pulmonary and systemic vasodilator effects of the newly discovered prostaglandin, PGI_2. J Appl Physiol 1978;45:408–13.
6. Kashani IA, Richardson B, Lammers RJ, Merritt TA, Bloor CM. Effects of prostaglandins on the pulmonary vascular bed of newborn rats with chronic hypoxia. Angiology 1986;37:21–5.
7. Dammenhayn L, Yagyu K, Schafers HJ, Haverich A. The effect of prostacyclin on reperfusion injury after pulmonary ischemia. Transplant Proc 1989;21:1363.
8. Hooper TL, Thomson DS, Jones MT, et al. Amelioration of lung ischemic injury with prostacyclin. Transplantation 1990;49:1031–5.
9. Bolanowski PJP, Bauer J, Machiedo G, Neville WE. Prostaglandin influence on pulmonary intravascular leukocytic aggregation during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1977;73:221–4.
10. Arima T, Gennda T, Ueda K, Hatanaka M, Omoto R, Matsumoto I. The effects of a prostacyclin analog OP-41483 on pulmonary oxygen toxicity in an isolated heart-lung autoperfusion model. Prostaglandins 1989;37:33–51.
11. Ueda K, Hatanaka M, Kyo S, et al. Effect of prostacyclin analog on pulmonary edema in isolated heart-lung autoperfusion model. J Heart Transplant 1987;6:155–61.
12. Miyamoto Y, Lajos TZ, Bhayana JN, Bergsland J, Celik CF. Beneficial effects of prostaglandin E1 on autoperfused heart-lung preservation. J Heart Transplant 1988;7:135–9.
13. Mashburn JP, Kontos GJ, Hashimoto K, Wilson DM, Schaff HV. The role of neural and vasoactive mediators in the regulation of the pulmonary circulation during cardiopulmonary preservation. J Thorac Cardiovasc Surg 1989;98.434–43.
14. Jones G, Hurley JV. The effect of prostacyclin on the adhesion of leucocytes to injured vascular endothelium. J Pathol 1984;142:51–9.
15. Vane JR. Adventures and excursions in bioassay—the stepping stones to prostacyclin. Postgrad Med J 1983;59:743–58.
16. Fantone JC, Marasco WA, Elgas LJ, Ward PA. Stimulus specificity of prostaglandin inhibition of rabbit polymorphonuclear leukocyte lysosomal enzyme release and superoxide anion production. Am J Pathol 1984;115:9–16.
17. Fantone JC, Funkel SL, Ward PA, Zurier RB. Suppression by

prostaglandin E1 of vascular permeability induced by vasoactive inflammatory mediators. J Immunol 1980;125:2591–6.

18. Patterson GA, Cooper JD. Status of lung transplantation. Surg Clin North Am 1988;68:545–58.
19. Harjula ALJ, Baldwin JC, Stinson EB, Oyer PE, Shumway NE. Clinical heart-lung preservation with prostaglandin E-1. Transplant Proc 1987;19:4101–2.
20. Harjula ALJ, Starkey TD, Hagberg RC, Baldwin JC. Intravenous prostaglandin E1, cold crystalloid flush and topical hypothermia for cardiopulmonary graft preservation. Ann Chir Gynaecol 1987;76:56–60.
21. Baldwin JC, Frist WH, Starkey TD, et al. Distant graft procurement for combined heart and lung transplantation using pulmonary artery flush and simple topical hypothermia for graft preservation. Ann Thorac Surg 1987;43:670–3.
22. Starnes VA, Baldwin JC, Harjula A. Combined heart and lung transplantation: the Stanford experience. J Appl Cardiol 1987;2:71–89.
23. Zenati M, Dowling RD, Armitage JM, et al. Organ procurement for pulmonary transplantation. Ann Thorac Surg 1989; 48:882–6.
24. Harjula ALJ, Baldwin JC, Silverman NE, et al. Implantation response following clinical heart-lung transplantation. J Cardiovasc Surg 1990;31:1–6.
25. Hakim M, Higenbottam T, English TAH, Wallwork J. Distant procurement and preservation of heart-lung homografts. Transplant Proc 1987;19:3535–6.
26. Hakim M, Higenbottam T, Bethune D, et al. Selection and procurement of combined heart and lung grafts for transplantation. J Thorac Cardiovasc Surg 1988;95:474–9.
27. Wallwork J, Jones K, Cavarocchi N, Hakim M, Higenbottam T. Distant procurement of organs for clinical heart-lung transplantation using a single-flush technique. Transplantation 1987;44:654–8.
28. Kirk AJB, Cooris PA, Conacher I, McGregor CGA, Dark JH. Clinical results with a flush-perfusion method of lung preservation. J Heart Transplant 1989;8:92.
29. Mulvin D, Jones K, Howard R, Grosso M, Repine J. The effect of prostacyclin as a constituent of a preservation solution in protecting lungs from ischemic injury because of its vasodilatory properties. Transplantation 1990;49:828–30.
30. Cremer J, Jurmann M, Dammenhayn L, Wahlers T, Haverich A, Borst HG. Oxygen free radical scavengers to prevent pulmonary reperfusion injury after heart-lung transplantation. J Heart Transplant 1989;8:330–6.
31. Locke TJ, Hooper TL, Flecknell PA, McGregor CGA. Preservation of the lung: comparison of topical cooling and cold crystalloid pulmonary perfusion. J Thorac Cardiovasc Surg 1988;96:789–95.
32. Jurmann MJ, Dammenhayn L, Schafers HJ, Wahlers T, Fieguth HG, Haverich A. Prostacyclin as an additive to single crystalloid flush: improved pulmonary preservation in heart-lung transplantation. Transplant Proc 1987;19:4103–4.
33. Hooper TL, Fetherston GJ, Flecknell PA, Dark JH, McGregor CGA. The use of a prostacyclin analog, Iloprost, as an adjunct to pulmonary preservation with Euro-Collins solution. Transplantation 1990;49:495–9.
34. Klepetko W, Muller MR, Khunl-Brady G, et al. Beneficial effect of Iloprost on early pulmonary function after lung preservation with modified Eurocollins solution. Thorac Cardiovasc Surg 1989;37:174–9.
35. Baldwin JC, Harjula A, Starkey TD, Jamieson SW, Shumway NE. Improved heart-lung graft preservation with prostaglandin E-1. J Am Coll Cardiol 1987;9:29A.
36. Harjula ALJ, Baldwin JC. Lung transplantation in the pig with successful preservation using prostaglandin E-1. J Appl Cardiol 1987;2:397–402.
37. Harjula A, Baldwin JC, Shumway NE. Donor deep hypothermia or donor pretreatment with prostaglandin E1 and single pulmonary artery flush for heart-lung graft preservation: an experimental primate study. Ann Thorac Surg 1988; 46:553–5.
38. Fraser CD, Tamura F, Adachi H, et al. Donor core-cooling provides improved static preservation for heart-lung transplantation. Ann Thorac Surg 1988;45:253–7.
39. Harjula ALJ, Baldwin JC, Shumway NE. Single lung transplantation in primates: modified Stanford heart-lung transplantation technique. Scand J Thorac Cardiovasc Surg 1989; 23:201–4.
40. Lehtola A, Harjula A, Heikkila L, et al. Single-lung allotransplantation in pigs following donor pretreatment with intravenous prostaglandin E-1: morphologic changes after preservation and reperfusion. Scand J Thorac Cardiovasc Surg 1989;23:193–9.
41. Bonser RS, Fragomeni LS, Jamieson SW, et al. The use of PGE-1 in 12 hour lung preservation. J Heart Transplant 1990;9:70.
42. Bonser RS, Fragomeni LS, Jamieson SW, Kaye MP. Deleterious effects of prostaglandin E1 in 12 hour lung preservation. Br Heart J 1989;61:463.
43. Haverich A, Scott WC, Aziz S, Jamieson S. Influence of perfusate flow and volume on preservation of the lungs for transplantation. Heart Transplant 1985;4:129.
44. Haverich A, Aziz S, Scott WC, Jamieson SW, Shumway NE. Improved lung preservation using Euro-Collins solution for flush-perfusion. Thorac Cardiovasc Surg 1986;34:368–76.
45. Yamazaki F, Yokomise H, Keshavjee SH, et al. The superiority of an extracellular fluid solution over Euro-Collins' solution for pulmonary preservation. Transplantation 1990; 49:690–4.
46. Yokomise H, Ueno T, Yamazaki F, Keshavjee S, Slutsky A, Patterson G. The effect and optimal time of administration of verapamil on lung preservation. Transplantation 1990;49: 1039–43.
47. Jones MT, Hsieh C, Yoshikawa K, Patterson GA, Cooper JD. A new model for assessment of lung preservation. J Thorac Cardiovasc Surg 1988;96:608–14.
48. Starkey TD, Sakakibara N, Hagberg RC, Tazelaar HD, Baldwin JC, Jamieson SW. Successful 6-hour cardiopulmonary preservation with simple hypothermic crystalloid flush. J Heart Transplant 1986;5:291–7.
49. Unruh H, Hoppensack M, Oppenheimer L. Vascular properties of canine lungs perfused with Eurocollins solution and prostacyclin. Ann Thorac Surg 1990;49:292–8.
50. Koyama I, Toung TJK, Rogers MC, Gurtner GH, Traystman RJ. O_2 radicals mediate reperfusion lung injury in ischemic O_2-ventilated canine pulmonary lobe. J Appl Physiol 1987;63: 111–5.
51. McCord JM, Fridovich I. The biology and pathology of oxygen radicals. Ann Intern Med 1978;89:122–7.
52. Frank L, Massaro D. Oxygen toxicity. Am J Med 1980;69:117–26.
53. Faymonville ME, Deby-Dupont G, Larbuisson R, et al. Prostaglandin E_2, prostacyclin, and thromboxane changes during nonpulsatile cardiopulmonary bypass in humans. J Thorac Cardiovasc Surg 1986;91:858–66.
54. Golub M, Zia P, Matsuno M, Horton R. Metabolism of prostaglandins A_1 and E_1 in man. J Clin Invest 1975;56:1404–10.
55. Moncada S, Gryglewski R, Bunting S, Vane JR. An enzyme isolated from arteries transforms prostaglandin endoperoxides to an unstable substance that inhibits platelet aggregation. Nature 1976;263:663–5.

KEY REFERENCES

Atrioventricular Canal Defects

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Morphology

1. Van Mierop LHS, Alley RD, Kausel HW, Stranahan A. The anatomy and embryology of endocardial cushion defects. J Thorac Cardiovasc Surg 1962;43:71–83.

   Based on a study of 21 graded and serially sectioned human embryos, the embryology of the normal endocardial cushion is detailed. Forty-six autopsy specimens are also analyzed to illustrate the pathogenesis of abnormal endocardial cushion development.

2. Van Mierop LHS, Alley RD. The management of the cleft mitral valve in endocardial cushion defects. Ann Thorac Surg 1966;2:416–23.

   The pathological anatomy and functional significance of the cleft mitral valve in endocardial cushion defects is discussed. The authors conclude that in many cases it is unnecessary to suture the cleft and it may be contraindicated in cases where there is little or no insufficiency. We prefer to suture the cleft in most cases.

3. Rastelli G, Kirklin JW, Titus JL. Anatomic observations on complete form of persistent common atrioventricular canal with special reference to atrioventricular valves. Mayo Clin Proc 1966;41:296–308.

   This classic article describes the pathological anatomy of this lesion and for the first time introduces the classification of Rastelli. From the examination of 30 hearts, the authors define three forms of complete atrioventricular canal, types A, B, and C, based on the anatomy of the anterior leaflet of the common valve. Recognition of these subdivisions has diagnostic and surgical importance.

4. Piccoli GP, Gerlis LM, Wilkinson JL, Lozsadi K, Macartney FJ, Anderson RH. Morphology and classification of atrioventricular defects. Br Heart J 1979;42:621–32.

   Anatomical analysis was made of 114 autopsy specimens in an attempt to clarify areas of disagreement in the characterization of atrioventricular canal defects. Based on their findings, the authors suggest that the group of anomalies termed intermediate types are best considered as variants of the partial form of atrioventricular canal.

5. Piccoli GP, Wilkinson JL, Macartney FJ, Gerlis L, Anderson RH. Morphology and classification of complete atrioventricular defects. Br Heart J 1979;42:633–9.

   This pathological study offers a modification of the Rastelli classification. Anatomical studies were made on 70 autopsied hearts with complete atrioventricular defects in an effort to subdivide the classification based on the morphology of the valve leaflets. The authors suggest that complete atrioventricular defects can be divided according to the attachment of the anterior leaflets of the valve.

6. Bharati S, Kirklin JW, McAllister HA, Lev M. The surgical anatomy of common atrioventricular orifice associated with tetralogy of Fallot, double outlet right ventricle and complete regular transposition. Circulation 1980;61:1142–9.

   Of 507 specimens with atrioventricular canal defects studied, 30 had tetralogy of Fallot, 34 double-outlet right ventricle, and 17 complete transposition. When associated with tetralogy or double-outlet right ventricle, the atrioventricular defect was of the complete type in 93% and the intermediate type in 7%. With the exception of 1 case, transposition was associated with the complete type of atrioventricular defect.

7. Piccoli GP, Ho SY, Phil M, et al. Left-sided obstructive lesions in atrioventricular septal defects. An anatomic study. J Thorac Cardiovasc Surg 1982;83:453–60.

   This report examines the potential factors predisposing to either inflow or outflow obstruction at the level of the left atrioventricular valve. Twenty-nine percent of 114 autopsied specimens with atrioventricular defects demonstrated unequivocal anatomical left-sided obstruction, which must be considered when planning surgical repairs.

8. Becker AE, Anderson RH. Atrioventricular septal defects: what's in a name? J Thorac Cardiovasc Surg 1982;83:461–9.

   The authors emphasize that optimal surgical repair of atrioventricular defects is based on an understanding of the abnormal septal morphology together with the malformed atrioventricular valve apparatus. Management of this spectrum of defects cannot be based on the normal morphology of the atrioventricular septum and valves, which cannot be reconstituted.

9. Thiene G, Wenink ACG, Frescura C, et al. Surgical anatomy and pathology of the conduction tissues in atrioventricular defects. J Thorac Cardiovasc Surg 1981;82:928–37.

   Sixteen hearts with atrioventricular defects were examined from a surgical standpoint in an attempt to define the anatomy of the conduction tissues that are at risk for injury during surgical repair. The anatomy of the normal triangle of Koch was distorted in all cases, and a separate posterior nodal triangle is defined that is the landmark for the atrioventricular node. Techniques are suggested for avoiding injury to atrioventricular conduction axis.

10. Anderson RH, Zuberbuhler JR, Penkoske PA, Neches WH. Of clefts, commissures, and things. J Thorac Cardiovasc Surg 1985;90:605–10.

    The authors discuss the nature of the breaches in the valve leaflet tissue guarding the atrioventricular junction in endocardial cushion defects. They propose that these breaches, traditionally known as clefts, are better described as commissures, which are functionally important in a trifoliate left atrioventricular valve.

11. Penkoske PA, Neches WH, Anderson RH, Zuberbuhler JR. Further observations on the morphology of atrioventricular septal defects. J Thorac Cardiovasc Surg 1985;90:611–22.

    Based on measurements of the junctional circumference of the left atrioventricular valve leaflets and ventricular dimensions, the authors compare a spectrum of lesions ranging from complete atrioventricular defects to isolated clefts of the mitral valve to determine which lesions should be categorized as atrioventricular canal defects. They emphasize the trifoliate structure of the left atrioventricular valve, which is morphologically different from the normal mitral valve in terms of its leaflet, chordal support, and arrangement of its papillary muscle.

12. Newfield EA, Sher M, Paul MH, Nikaidoh H. Pulmonary vascular disease in complete atrioventricular canal defect. Am J Cardiol 1977;39:721–6.

    This article examines the incidence and time of occurrence of pulmonary vascular disease in 67 children with complete atrioventricular canal. Palliative or corrective operation was recommended

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before age 1 year to prevent development of advanced pulmonary vascular disease. We prefer repair before 6 months of age.

13. Berger TJ, Blackstone EH, Kirklin JW, Bargeron LM, Hazelrig JB, Turner ME. Survival and probability of cure without and with operation in complete atrioventricular canal. Ann Thorac Surg 1979;27:104–11.

    Only 54% of patients with complete atrioventricular canal survived to 6 months of age without operation, indicating urgent early repair may be necessitated by the natural history of the disease. Although the risk of correction is higher in the early months of life, 5-year survival rate among patients leaving the hospital after repair was 91%.

Technique of Operation (without major associated cardiac anomaly)

14. Rastelli GC, Ongley PA, Kirklin JW, McGoon DC. Surgical repair of the complete form of persistent common atrioventricular canal. J Thorac Cardiovasc Surg 1968;55:299–308.

    In this classic paper the authors discuss their technique for the repair of complete atrioventricular canal between 1955 and 1967. The single-patch technique they used later in their series with reduced hospital mortality involves reattachment of the mitral valve structures to the septal patch at the normal anatomical position. Unlike previous techniques, this modification preserved an adequate left ventricular outflow tract and allowed adequate valve function.

15. Rastelli GC, Ongley PA, McGoon DC. Surgical repair of complete atrioventricular canal with anterior common leaflet undivided and unattached to ventricular septum. Mayo Clin Proc 1969;44:335–41.

    The technique used for repairing this variation of complete atrioventricular canal is described. A single-patch technique is used after appropriately incising the undivided anterior common leaflet.

16. Katz NM, Blackstone EH, Kirklin JW, Bradley EL, Lemons JE. Suture techniques for atrioventricular valves: experimental study. J Thorac Cardiovasc Surg 1981;81:528–36.

    This canine study attempts to determine the optimal suture technique for avoiding dehiscence of sutured atrioventricular valves. The authors conclude that suture line strength is increased by load-distributing techniques such as buttressing with pledgets or using deep, narrowly spaced bites.

17. Moreno-Cabral RJ, Shumway NE. Double-patch technique for correction of complete atrioventricular canal. Ann Thorac Surg 1982;33:88–91.

    The authors describe the double-patch technique they perform entirely through a right atriotomy. A crescent-shaped Teflon patch is used for closure of the ventricular defect and resuspension of the atrioventricular valves. A separate pericardial patch is used to close the atrial defect.

18. Bove EL, Sondheimer HM, Kavey RW, Byrum CJ, Blackman MS. Results with the two-patch technique for repair of complete atrioventricular septal defect. Ann Thorac Surg 1984;38:157–60.

    Nine patients underwent repair of complete atrioventricular defects using a double-patch technique. The authors conclude that by using separate atrial and ventricular patches less distortion is created, allowing a more accurate reconstruction of a competent trileaflet mitral valve.

19. Santos A, Boucek M, Ruttenberg H, Veasy G, Orsmond G, McGough E. Repair of atrioventricular septal defects in infancy. J Thorac Cardiovasc Surg 1986;91:505–10.

    This report recommends the use of ventricular distention during operative repair to minimize distortion and improve accuracy in reconstruction of the trileaflet mitral valve. The authors conclude that if ventricular distention is used, the double-patch technique offers no advantage over the single-patch repair.

20. Pan-Chih, Chen-Chun. Surgical treatment of atrioventricular canal malformations. Ann Thorac Surg 1987;43:150–4.

    In this series a single-patch technique was used for repair of complete atrioventricular defects. The authors recommend partial approximation of the mitral cleft when intraoperative assessment indicates the presence of a regurgitant jet.

21. Urban AE. Total correction of complete atrioventricular canal: surgical techniques and analysis of long-term results. Prog Pediatr Surg 1990;25:118–22.

    The double-patch technique was used for repair of complete atrioventricular septal defects. In an attempt to avoid postrepair atrioventricular valve incompetence, the authors have modified their original technique by routinely closing the cleft with interrupted sutures in all cases.

Technique of Operation (with major associated cardiac anomaly)

22. Alfieri O, Plokker M. Repair of common atrioventricular canal associated with transposition of the great arteries and left ventricular outflow obstruction. J Thorac Cardiovasc Surg 1982;84:872–5.

    The authors outline the procedure, which involves closure of the atrioventricular canal, partitioning of the common atrioventricular orifice, performance of a Mustard operation, and insertion of a valved conduit between the left ventricle and pulmonary artery. Because this operation leads to a four-chambered heart, it may be preferable to the previously described Fontan type of repair.

23. Gow RM, Freedom RM, Williams WG, Trusler GA, Rowe RD. Coarctation of the aorta or subaortic stenosis with atrioventricular septal defect. Am J Cardiol 1984;53:1421–8.

    The surgical management of 30 patients with atrioventricular defects and either subaortic stenosis or coarctation of the aorta or both is discussed. Complete repair with coarctation can be accomplished using the subclavian flap technique. The presence of subaortic stenosis requires excision of the obstruction to the left ventricular outflow tract.

24. Uretzky G, Puga FJ, Danielson GK, et al. Complete atrioventricular canal associated with tetralogy of Fallot: morphologic and surgical considerations. J Thorac Cardiovasc Surg 1984;87:756–66.

    A single-patch technique was used for repair through the atrial approach alone or a combined atrial and right ventricular approach. Seven of 14 patients underwent transannular patching without pulmonic valve replacement, and no increase was seen in early or late mortality.

25. Vouhe PR, Neveux JY. Surgical repair of tetralogy of Fallot with complete atrioventricular canal. Ann Thorac Surg 1986;41:342–4.

    This report outlines the authors' technique of repair, which involves a combined right atrial and right ventricular approach, double-patch closure of the septal defects, and functional repair of the newly constructed mitral valve. Infundibular and valvar pulmonary stenosis are corrected through the longitudinal right ventriculotomy.

26. Vargas FJ, Coto EO, Mayer JE, Jonas RA, Castaneda AR. Complete atrioventricular canal and tetralogy of Fallot: surgical considerations. Ann Thorac Surg 1986;42:258–63.

    The authors describe modifications of technique that may be useful in the surgical management of the anatomical variations in atrioventricular canal associated with tetralogy of Fallot. Because of the anterior-superior displacement of the conal septum, atrioventricular valve reconstruction may produce subaortic narrowing and obstruc-

tion. By obliquely dividing the anterior leaflet and following the crest of the malaligned septum, narrowing of the outflow tract is avoided.

27. Pacifico AD, Ricchi A, Bargeron LM, Colvin EC, Kirklin JW, Kirklin JK. Corrective repair of complete atrioventricular canal defects and major associated cardiac anomalies. Ann Thorac Surg 1988;46:645–51.

    Twenty-nine patients with complete atrioventricular canal defects and major associated cardiac anomalies underwent corrective repair using a double-patch technique. Twenty-three of 25 patients with ventriculoarterial concordant or double-outlet connections required construction of an intraventricular tunnel connecting the left ventricle with the aorta.

Special Situations and Controversies

Pulmonary Artery Banding

28. Epstein ML, Moller JH, Amplatz K, Nicoloff DM. Pulmonary artery banding in infants with complete atrioventricular canal. J Thorac Cardiovasc Surg 1979;78:28–31.

    Pulmonary artery banding provided effective palliation for infants with complete atrioventricular canal and congestive heart failure who had large ventricular shunts and minimal mitral insufficiency. Complete repair is advocated for infants with severe mitral insufficiency who fail to respond to medical management as pulmonary banding was uniformly fatal.

29. Kirklin JW, Blackstone EH. Management of the infant with complete atrioventricular canal. J Thorac Cardiovasc Surg 1979;78:32–4.

    This editorial reviews the data from a previous study that supported pulmonary banding in selected infants with complete atrioventricular canal defects. The authors conclude that primary repair should be the treatment of choice for complete atrioventricular canal defect in small infants.

30. Silverman N, Levitsky S, Fisher E, Dubrow I, Hastreiter A, Scagliotti D. Efficacy of pulmonary banding in infants with complete atrioventricular canal. Circulation 1983;68(Suppl 2):148–53.

    Pulmonary artery banding was performed on 21 consecutive infants with complete atrioventricular canal and congestive heart failure with a 4.7% in-hospital mortality. The authors conclude that pulmonary artery banding is a rational alternative to complete repair, which in previous reports carried a significantly higher risk.

31. Williams WH, Guyton RA, Michalik RE, et al. Individualized surgical management of complete atrioventricular canal. J Thorac Cardiovasc Surg 1983;86:838–44.

    Based on their experience with 46 patients, the authors recommend total correction of complete atrioventricular canal in infants and children weighing more than 4 to 5 kg. For infants weighing less, the pulmonary artery is initially banded and anatomical repair is performed during the second year of life.

Atrioventricular Canal in Adults

32. Hynes JK, Tajik AJ, Seward JB, et al. Partial atrioventricular canal defect in adults. Circulation 1982;66:284–7.

    Forty-seven patients aged 20 years or older underwent surgical repair of partial atrioventricular canal defects with a 6.4% operative mortality and a 4.3% late mortality. The authors conclude that repair of partial atrioventricular canal in adults may be performed at low risk and may improve longevity and functional status.

Down's Syndrome and Atrioventricular Canal

33. Clapp S, Perry BL, Farooki ZQ, et al. Down's syndrome, complete atrioventricular canal, and pulmonary vascular obstructive disease. J Thorac Cardiovasc Surg 1990;100:115–21.

    The authors reviewed their experience over a 10-year period and concluded that Down's syndrome patients with complete atrioventricular canal develop pulmonary vascular obstructive disease earlier than children with normal chromosomes. Consequently, especially in those patients with Down's syndrome, cardiac catheterization with estimation of pulmonary vascular resistance should be performed before 6 months of age.

Early Results

34. McMullan MH, McGoon DC, Wallace RB, Danielson GK, Weidman WH. Surgical treatment of partial atrioventricular canal. Arch Surg 1973;107:705–10.

    Hospital mortality was 5.6% in this series of 141 patients who underwent repair of partial atrioventricular canal defects. Analysis of data suggested that infancy and large heart size had an unfavorable influence on operative risk, and severity of symptoms had borderline significance.

35. Mair D, McGoon DC. Surgical correction of atrioventricular canal during the first year of life. Am J Cardiol 1977;40:66–9.

    Definitive repair of atrioventricular canal defects in 8 infants less than 1 year of age was performed because of intractable congestive heart failure. Six of 8 patients were alive and well at follow-up, demonstrating that complete correction is possible in small infants with an excellent chance for success.

36. Berger TJ, Kirklin JW, Blackstone EH, Pacifico AD, Kouchoukos NT. Primary repair of complete atrioventricular canal in patients less than 2 years old. Am J Cardiol 1978;41:906–13.

    Hospital mortality was 19% for patients operated on after January 1, 1975, versus 73% who died after operation between 1972 and 1975. Age at operation, anatomical variations, and technique of profound hypothermia were not related to mortality. Increased survival was attributed to improved ability to reconstruct the atrioventricular valves.

37. Chin AJ, Keane JF, Norwood WI, Castaneda AR. Repair of complete common atrioventricular canal in infancy. J Thorac Cardiovasc Surg 1982;84:437–45.

    Operative mortality in a series of 43 infants was 62% between January 1, 1975, and June 30, 1980, compared with an operative mortality of 17% from 1978 to 1980. Several anatomical features influenced the outcome of reparative procedures, making a uniform approach to valve reconstruction impossible.

38. Bender HW, Hammon JW, Hubbard SG, Muirhead J, Graham TP. Repair of atrioventricular canal malformation in the first year of life. J Thorac Cardiovasc Surg 1982;84:515–22.

    Twenty-four consecutive infants (average age, 18 weeks) with atrioventricular canal defects and refractory heart failure underwent surgical repair with an operative mortality of 8%. Based on these results, the authors feel that complete repair in infancy is safe and avoids unnecessary delay, which may allow the progression of pulmonary vascular disease.

39. Studer M, Blackstone EH, Kirklin JW, et al. Determinants of early and late results of repair of atrioventricular septal (canal) defects. J Thorac Cardiovasc Surg 1982;84:523–42.

    The authors retrospectively reviewed the anatomical and functional characteristics of 310 patients who underwent repair of atrioventricular septal defects between 1967 and 1982. Currently, significant incremental risk factors for hospital death include: severity of preoperative atrioventricular valve incompetence, in-

creased level of preoperative functional class, presence of interventricular communication, and presence of accessory valve orifices.

40. Rizzoli G, Mazzucco A, Brumana T, et al. Operative risk of correction of atrioventricular septal defects. Br Heart J 1984; 52:258–65.

    In this series of 111 patients who underwent surgical repair for atrioventricular canal, 43 had the complete, 11 the intermediate, and 57 the partial form, and the early mortality was 37%, 9%, and 6%, respectively. Operative risk was primarily related to failure to obtain a well functioning atrioventricular valve, presence of left ventricular dominance, degree of pulmonary vascular resistance, and technique of reconstructing a two-leaflet left atrioventricular valve.

41. Castaneda AR, Mayer JE, Jonas RA. Repair of complete atrioventricular canal in infancy. World J Surg 1985;9:590–7.

    Using a single-patch technique, the authors report an early mortality of 6.2% in this series of 48 patients undergoing repair of complete atrioventricular canal defects from July 1980 through July 1984. Improved surgical results are attributed to: advances in preoperative, intraoperative, and postoperative care; better understanding of the relevant pathological factors, especially of the left atrioventricular valve; clearer definition of the path of the conduction tissue; and the recognition of associated defects.

42. Clapp SK, Perry BL, Farooki ZQ, et al. Surgical and medical results of complete atrioventricular canal: a ten year review. Am J Cardiol 1987;59:454–8.

    The authors reviewed the surgical and medical management of 121 patients seen over a 10-year period to determine overall prognosis. The early mortality of 30% in the operated group reflects frequently unfavorable anatomy such as hypoplastic ventricle, double-orifice mitral valve, deficiency of mitral tissue, or pulmonary vascular obstructive disease.

43. Baciewicz FA, Melvin WS, Basilius D, Davis JT. Congenital heart disease in Down's syndrome patients: a decade of surgical experience. Thorac Cardiovasc Surg 1989;37:369–71.

    Eighteen of 26 patients in this series with Down's syndrome and atrioventricular canal underwent initial surgical repair with a 16.7% 30-day mortality versus a 37.5% mortality for those having pulmonary artery banding and a later corrective operation. The population with Down's syndrome did not exhibit an increased surgical risk compared with patients without Down's syndrome.

Late Results

44. Lillehei CW, Anderson RC, Ferlic RM, Bonnabeau RC. Persistent common atrioventricular canal: recatheterization results in 37 patients following intracardiac repair. J Thorac Cardiovasc Surg 1969;57:83–94.

    Thirty-seven patients ranging in age from 17 months to 47 years were recatheterized 2 months to 11 years after surgical repair of atrioventricular canal. Results included: significant reduction in hypertension postoperatively, residual right to left shunt at the atrial level in 4 patients, and residual mitral valvar insufficiency in 4 patients.

45. Midgley FM, Galioto FM, Shapiro SR, Perry LW, Scott LP. Experience with repair of complete atrioventricular canal. Ann Thorac Surg 1980;30:151–9.

    In this series of 29 patients who underwent repair of complete atrioventricular canal, four of five late deaths were caused by infection, and the other occurred in a 2-year-old patient at the time of reoperation for mitral valve replacement. In those patients studied, follow-up catheterization demonstrated pulmonary vascular resistance values to be essentially unchanged from preoperative levels.

46. King RM, Puga FJ, Danielson GK, Schaff HV, Julsrud PR, Feldt RH. Prognostic factors and surgical treatment of partial atrioventricular canal. Circulation 1986;74(Suppl 1):42–6.

    Between January 1962 and January 1984, 199 patients underwent correction of partial atrioventricular canal with a 96% late survival (mean follow-up, 15.2 years). Reoperation was necessary on 15 patients for mitral incompetence and 3 patients for subaortic stenosis. Need for reoperation correlated with severity of postrepair mitral regurgitation.

47. Stewart S, Alexson C, Manning J. Partial atrioventricular canal defect: the early and late results of operation. Ann Thorac Surg 1987;43:527–9.

    There were no late deaths among the 35 patients in this series followed up for a mean of 8 years. Based on their excellent long-term results, the authors recommend treatment of the mitral valve as a bileaflet structure with closure of the cleft in the anterior leaflet when the valve is incompetent.

48. McGrath LB, Gonzalez-Lavin L. Actuarial survival, freedom from reoperation, and other events after repair of atrioventricular septal defects. J Thorac Cardiovasc Surg 1987;94:582–90.

    Operative technique in this series was based on a trifoliate concept of the left atrioventricular valve with performance of cleft suture and annuloplasty only as necessary. Late reoperation was required in 11% of patients after repair of partial atrioventricular septal defects and in 24% with complete defects. The preoperative severity of left atrioventricular valve incompetence was not found to be a significant risk factor for late reoperation.

49. Ceithaml EL, Midgley FM, Perry LW. Long-term results after surgical repair of incomplete endocardial cushion defects. Ann Thorac Surg 1989;48:413–6.

    Mean follow-up was 7 years in this series of 56 patients who underwent surgical repair of incomplete endocardial cushion defects between 1964 and 1986. There were three late deaths (5.7%), and 12 patients (22.6%) required additional operations. Twenty-eight percent of patients who demonstrated moderate to severe mitral regurgitation on preoperative cardiac catheterization ultimately required mitral valve replacement.

50. Pozzi M, Remig J, Fimmers R, Urban AE. Atrioventricular septal defects. Analysis of short- and medium-term results. J Thorac Cardiovasc Surg 1991;101:138–42.

    Of those who survived the initial operation, 10.9% required reoperation for atrioventricular valve repair failure. Since the authors have modified their technique to include suture of the cleft to create a bileaflet valve whenever feasible, no episodes of valve repair failure have occurred. Preoperative severity of atrioventricular valve incompetence was a risk factor for requiring reoperation in this series.

Pharmacological Response of Internal Mammary Artery and Gastroepiploic Artery

To the Editor:

We read with interest the recent article by Koike and associates [1] concerning the response of the internal mammary artery (IMA) and gastroepiploic artery to ergonovine, serotonin, and phenylephrine. This response was examined by isometric contraction–recording apparatus. Koike and associates report no significant difference in developed tension between IMA and gastroepiploic artery at any concentration for any agent. However, their research rather studies a change in length of the conduit, whereas we think that, based on our observation of a spiral arrangement of smooth muscle in the media of muscular vessels, the pharmacological effects on the width of the conduit, ie, on the luminal diameter, may be more apparent.

In addition, Koike and associates did not specify from which section of the IMA the IMA specimens were obtained, although we assume that the examined specimens were harvested distally, because they were obtained during operation. In that case it would still be of utmost importance to know if they were obtained proximal to the epigastric bifurcation or distal to it. In a recent study we have documented a changing histological pattern of the IMA along its course up to the epigastric bifurcation and substantially different histological features of the IMA in comparison with its continuation into the superior epigastric artery and the musculophrenic artery [2]. In the majority of patients, in its first 5 cm, the media of the IMA is elastomuscular; beyond this section, up to approximately 3 to 4 cm proximal to the epigastric bifurcation, it is completely elastic. The last section, up to the epigastric bifurcation, is elastomuscular again. The very proximal sections of the superior epigastric artery and musculophrenic artery are muscular with rare elastic lamellae and subsequently are almost completely muscular.

These findings may have profound influence on the propensity to vasospasm of the underlying arterial graft. We hypothesize that vasospasm may be significantly more apparent in the elastomuscular sections of the IMA and its continuation into the muscular superior epigastric artery and musculophrenic artery. Our histological findings and hypothesis are in concordance with the findings of Kitamura and colleagues [3], who reported that the IMA is substantially less reactive to ergonovine than the muscular coronary artery (in analogy to the gastroepiploic artery) [4]. A study by He and colleagues [5] confirms our hypothesis of a limited reactivity of the IMA to sympathomimetic drugs. The discrepancy between the findings of Koike and co-workers and those of Kitamura and associates may probably be ascribed to research of the IMA at different histological levels and the fact that the former group studied the relation between pharmacological effect and length of the conduit, whereas the latter observed vasospasm, ie, luminal narrowing of the underlying vessel. Our hypothesis is also in agreement with the findings of Mills and Everson [6] and Suma [7], who reported a greater propensity to vasospasm of the muscular gastroepiploic artery than of the IMA. Generally, our data indicate that the IMA shows the histological features of an artery that both functions as a pressure reservoir and possesses a vasoregulatory capacity with regard to perfusion of the chest wall, the mammary gland, the diaphragm, and the rectus abdominis muscle.

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References

1. Koike R, Suma H, Kondo K, et al. Pharmacological response of internal mammary artery and gastroepiploic artery. Ann Thorac Surg 1990;50:384–6.
2. Van Son JAM, Smedts F, de Wilde PCM, et al. Histologic study to optimize selection of the anastomotic site in internal mammary artery for myocardial revascularization. J Thorac Cardiovasc Surg (in press).
3. Kitamura S, Morita R, Kawachi K, et al. Different responses of coronary artery and internal mammary artery bypass grafts to ergonovine and nitroglycerin in variant angina. Ann Thorac Surg 1989;47:756–60.
4. Van Son JAM, Smedts F, Vincent JG, van Lier HJJ, Kubat K. Comparative anatomic studies of various arterial conduits for myocardial revascularization. J Thorac Cardiovasc Surg 1990; 99:703–7.
5. He G, Buxton B, Rosenfeldt FL, Wilson AC, Angus JA. Weak β-adrenoceptor–mediated relaxation in the human internal mammary artery. J Thorac Cardiovasc Surg 1989;97:259–66.
6. Mills NL, Everson CT. Right gastroepiploic artery: a third arterial conduit for coronary artery bypass. Ann Thorac Surg 1989;47:706–11.
7. Suma H. Spasm of the right gastroepiploic artery. Ann Thorac Surg 1990;49:168–9.

Reply

To the Editor:

Gastroepiploic artery (GEA) graft has been reported by Mills and Everson [1] and Suma [2] to be more susceptible to vasospasm than internal mammary artery (IMA) graft, whereas we reported the pharmacological equivalence of those arterial conduits. Van Son and associates [3] reported the histological difference between IMA and GEA grafts: the former was elastic, but the latter was muscular. They also suggested that the histological difference might be one of the factors responsible for the spasmogenicity of GEA [4].

Our study [5] was done in an in vitro fashion using "helical" strips of the conduits, so there was no concern regarding humoral and/or neurological vasoconstriction factors. The developing tension in our results might be expressed as a complex of both the length and the width of the conduit, although "spasm" is defined as a transient luminal narrowing of the conduit.

The specimens were obtained during operation and the distal segments were used for experiments. Van Son and Smedts mentioned that the peripheral portion of IMA was elastomuscular or muscular, and that portion had a similar construction to GEA. We think that the distal portion of the arterial (IMA and GEA) grafts was used in this study.

We have performed a further examination to compare the response of the arterial (IMA and GEA) graft with that of saphenous vein graft and coronary artery using the same apparatus. Table 1 shows the 50% effective dose value of each agent

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Table 1. 50% Effective Dose Value[a]

Vessel	Ergonovine	Serotonin	Phenylephrine
IMA	5.1×10^{-8}	1.1×10^{-7}	1.6×10^{-6}
GEA	12.0×10^{-8}	2.9×10^{-7}	2.2×10^{-6}
SV	1.6×10^{-8}[b]	0.25×10^{-7}[c]	1.7×10^{-6}
Coronary artery	0.8×10^{-8}[b]	0.5×10^{-7}[c]	2.9×10^{-6}

[a] The 50% effective dose value was defined as the concentration of agent at which 50% of the maximum response was obtained. It was calculated by probit analysis to compare sensitivity. The less the value is, the more sensitive the vessel is to the agent. [b] $p < 0.05$ versus IMA. [c] $p < 0.01$ versus IMA.

IMA = internal mammary artery; GEA = gastroepiploic artery; SV = saphenous vein.

for each graft. The data suggest that the response of arterial grafts is entirely different from that of saphenous vein and coronary arteries: α_1-adrenergic stimulation produces almost equipotent contractions in these vessels, whereas serotonin and ergonovine induce more potent contractions in saphenous vein and coronary arteries than in IMA and GEA. So, IMA and GEA grafts seem to be unresponsive to the conditions that provoke coronary artery spasm. In postoperative angiography, Kitamura and associates [6] have reported that an IMA graft was not constricted in response to ergonovine, at least in the amount required to produce coronary artery spasm. Our data are in concordance with the report of Kitamura and associates. We also think arterial grafts will be the conduits of choice in patients with vasospastic angina from a pharmacological viewpoint.

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References

1. Mills NL, Everson CT. Right gastroepiploic artery: a third arterial conduit for coronary artery bypass. Ann Thorac Surg 1989;47:706–11.
2. Suma H. Spasm of the right gastroepiploic artery. Ann Thorac Surg 1990;49:168–9.
3. Van Son JAM, Smedts F, Vincent JG, van Lier HJJ, Kubat K. Comparative anatomic studies of various arterial conduits for myocardial revascularization. J Thorac Cardiovasc Surg 1990; 99:703–7.
4. Van Son JAM, Vincent JG. Spasm of arterial conduits in aorta–coronary bypass grafting. Ann Thorac Surg 1990;50: 1019.
5. Koike R, Suma H, Kondo K, et al. Pharmacological response of internal mammary artery and gastroepiploic artery. Ann Thorac Surg 1990;50:384–6.
6. Kitamura S, Morita R, Kawachi K, et al. Different responses of coronary artery and internal mammary artery bypass grafts to ergonovine and nitroglycerin in variant angina. Ann Thorac Surg 1989;47:756–60.

Mitral Valve Suture Techniques

To the Editor:

The recently published experimental study by Chambers and Heath [1] reaffirms previous laboratory work by Newton and associates [2]. The conclusion of these two studies is that it takes more force to cause left ventricular rupture or prosthetic valve dehiscence if horizontal mattress suture pledgets are placed on the ventricular side of the mitral valve annulus as compared with placing the pledgets on the atrial side of the annulus. Caution should be exercised, however, before translating these results to the implantation of pivoting disc valves in humans.

As pointed out by Starek and associates [3] in 1976, when pledgets are placed on the ventricular side of the mitral annulus during pivoting disc valve implantation, annular tissue may be forced against the valve providing impedance to disc motion. This may have been responsible for the increased incidence of Lillehei-Kaster valve thrombosis reported by this group. Starek [4] also demonstrated this problem photographically in his book. It appears that when the pledgets are placed supraannularly, there is eversion of the annulus so that annular tissue will not interfere with disc movement.

Unaware of Starek's work, several years ago I attempted to implant a 31-mm Medtronic-Hall mitral prosthesis using 1-0 Ethibond mattress sutures with the pledgets (Ethicon Teflon felt) placed on the ventricular side of the mitral valve annulus. Upon testing the disc for free movement, it was clear that annular tissue interfered with the movement of the disc, preventing it from fully opening and closing. The sutures were cut free, and the same valve was reimplanted using the same sized suture material and pledgets only this time with the pledgets situated on the atrial (supraannular) side of the mitral annulus. After this, free disc movement was present, and the patient has done well for more than 3 years.

Although only a single experience, this event and the work by Starek leads to the suggestion that caution be exercised when considering the subannular pledget technique for pivoting-disc mitral prosthetic valve implantation. It is noted that the manufacturer of the Medtronic-Hall valve also recommends avoiding the placement of pledgets on the ventricular side of the mitral valve annulus.

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References

1. Chambers EP, Heath BJ. Comparison of supraannular and subannular pledgeted sutures in mitral valve replacement. Ann Thorac Surg 1991;51:60–4.
2. Newton JR, Glower DD, Davis JW, Rankin JS. Evaluation of suture techniques for mitral valve replacement. J Thorac Cardiovasc Surg 1984;88:248–52.
3. Starek PJK, McLaurin LP, Wilcox BR, Murray GF. Clinical evaluation of the Lillehei-Kaster pivoting disc valve. Ann Thorac Surg 1976;22:362–8.
4. Starek PJK. Heart valve replacement and reconstruction. Chicago: Year Book Medical Publishers, 1987:72–3.

Reply

To the Editor:

I am in full agreement with Dr Lemmer that caution should be exercised when pledgets are placed on the ventricular side of the mitral annulus with the implantation of pivoting-disc valves. However, we now have more than 200 St. Jude mechanical valves in place using this technique in both the aortic and mitral positions. In no case has there been any impingement of valve leaflet mobility and there has been no known case of valve thrombosis. I agree that there is more concern when there is a larger disc movement as is the case with the Medtronic-Hall prosthesis, but the pledgets can clinically be placed such that there is no concern with this particular valve also. Several precautions can be taken, however, to ensure that there is no tissue or pledget material in the subannular area that might impose restriction to the leaflets.

First, the good flow characteristics of the St. Jude valve, and the Medtronic-Hall valve as well, allow one to select a size that is perhaps one size smaller than the largest valve that potentially could be implanted. This allows the pledget material and suture line to be further peripheral, allowing the implanted valve to sit somewhat in the annulus rather than further up on the rim of the annulus.

Second, small pledgets (3 to 6 mm firm Teflon) are used with 2-0 Ethicon sutures, and the bite taken in the sewing ring of the valve is kept peripheral and away from the metallic component. In the St. Jude valve placement this allows the pledget to pull outside the actual ring of pyrolytic carbon that houses the leaflets and their pathways of motion. When one looks down into the ventricle through the implanted valve, one sees no annular tissue or pledget material.

In conclusion, with only minor variations in the usual implantation techniques, I am fully convinced that any surgeon can apply this implantation technique with absolutely no risk of impingement of leaflet mobility, with what appears to be a much more securely seated valve, and with less likelihood of ventricular rupture. I have a very strong clinical impression that this implantation technique is even more important and more beneficial when implanting a valve in a redo annulus and in an annulus involved with subendocardial bacterial endocarditis.

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Continuous Warm Blood Cardioplegia

To the Editor:

I read with interest the recent article by James R. Kauten, MD, entitled "Easy cardioplegia delivery, aortic venting, and reperfusion techniques" [1].

Stimulated by published data on methods of blood cardioplegia for myocardial protection during open heart operations [2–4], our unit has adopted a simplified and, we believe, improved method for continuous delivery of oxygenated warm blood cardioplegia during the entire cross-clamping period. We employ a crystalloid prime for our normothermic perfusion. Cardiopulmonary bypass is established between an ascending aortic cannula and a two-stage atrial cannula, and the left ventricle is decompressed through the right superior pulmonary vein. An aortic root cannula (DLP Inc, Grand Rapids, MI) is secured to the ascending aorta and a multiple perfusion set (Shiley Inc, Irvine, CA), much like the one described by Kauten, is attached to the aortic root cannula. Air is removed from the system by flushing it progradely from the aortic root limb. This system is connected to a Shiley-B.C.D. Plus cardioplegia delivery unit, which yields a mixture of oxygenated blood (from the pump reservoir) and cardioplegia solution at a 4:1 ratio (Fig 1).

After aortic cross-clamping, oxygenated warm blood cardioplegia with a high potassium content (60 mEq/L) is delivered to the aortic root for 5 to 7 minutes at a pressure of 100 mm Hg and flows between 200 and 300 mL/min. When complete electromechanical arrest is produced, warm blood cardioplegia is continued with a low potassium content (20 mEq/L) and the first distal venous anastomosis is completed. Cardioplegia is delivered through the new graft, using one of the limbs of the multiperfusion set. This maneuver is repeated for any additional distal venous anastomosis. Finally, if the internal mammary artery is to be used, it is anastomosed as usual and flow is allowed to start through it.

With all distal anastomoses completed, the cardioplegic solution is halted and the aortic root and all venous grafts are perfused with warm blood to minimize the total amount of potassium delivery to the system. With a side-occluding clamp the proximal venous anastomoses are constructed, one at a time,

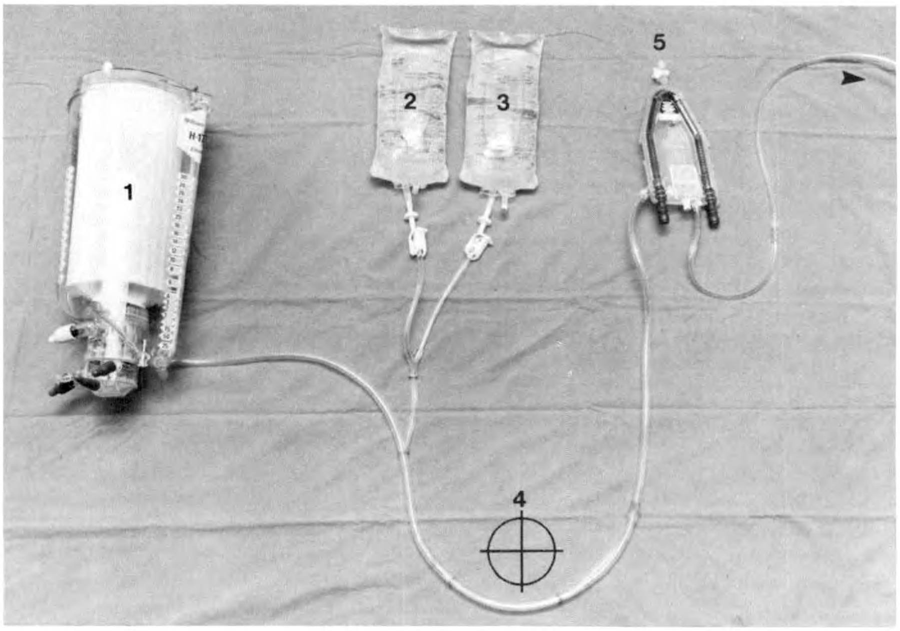

Fig 1. Continuous warm blood cardioplegia delivery system: (1) pump reservoir, (2) cardioplegia with high potassium content, (3) cardioplegia with low potassium content, (4) roller pump, and (5) Shiley-B.C.D. Plus cardioplegia system.

while the remaining venous grafts are being continuously perfused. At the conclusion of all proximal anastomoses, the heart has resumed sinus rhythm. The left ventricular sump is then removed and the patient is taken off cardiopulmonary bypass.

If retrograde coronary sinus perfusion is required, a retroplegia cannula (Gundry RCSP Cannula; DLP Inc) is connected to the cardioplegia delivery system described herein, and warm blood cardioplegia is delivered continuously to the coronary sinus at a pressure not exceeding 50 mm Hg and at a usual flow of 150 to 200 mL/min.

Since the implementation of this technique in March 1990, our results have been gratifying. This system offers, we think, the following advantages: (1) enhanced protection: warm blood cardioplegia is delivered continuously to the aortic root-venous grafts or to the coronary sinus for uninterrupted myocardial protection throughout the period of aortic cross-clamping; (2) simplicity: the set-up is assembled with readily available commercial equipment and requires minimal manipulation once in place; and (3) versatility: the system allows for uninterrupted prograde or retrograde cardioplegia as the patient's condition may dictate.

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References

1. Kauten JR. Easy cardioplegia delivery, aortic venting, and reperfusion technique. Ann Thorac Surg 1990;50:833–5.
2. Bomfim V, Kaijser L, Bendz R, et al. Myocardial protection during aortic valve replacement. Cardiac metabolism and enzyme release following continuous blood cardioplegia. Scand J Thorac Cardiovasc Surg 1983;86:507–18.
3. Rosenkranz ER, Buckberg GD, Laks H, Mulder DG. Warm induction of cardioplegia with glutamate-enriched blood in coronary patients with cardiogenic shock who are dependent on inotropic drugs and intra-aortic balloon support. J Thorac Cardiovasc Surg 1983;86:507–18.
4. Panos A, Christakis GT, Lichtenstein SV, Wittnich C, El-Dalati H, Salerno TA. Operation for acute postinfarction mitral insufficiency using continuous oxygenated blood cardioplegia. Ann Thorac Surg 1989;48:816–9.

Electrocardiography in Postbypass Patients

To the Editor:

Temporary transthoracic epicardial pacemaker leads are frequently placed in patients undergoing open heart operations. These leads can be helpful both diagnostically and therapeutically. However, in at least one circumstance, the presence of these leads can result in diagnostic confusion.

A 60-year-old man had aortocoronary bypass grafting to four vessels without incident. The patient had suffered a myocardial infarction with heart failure but there was no enzymatic evidence of perioperative infarction. Until the fourth day, the postoperative electrocardiogram had shown no change. There was evidence of the previous anterior infarction with slight ST elevation in the anteroseptal leads. On the fourth postoperative day, the electrocardiogram showed new, isolated, ST elevation of 9 mm in lead V_3 (Fig 1). The other 11 leads were unchanged. There was no clinical evidence of myocardial infarction. On the fifth postoperative day the electrocardiogram reverted to the baseline pattern (Fig 2). There remained no enzymatic or clinical evidence of myocardial infarction. It is postulated that the isolated "current of injury" on the fourth postoperative day was the result of electrical contact between the V_3 lead and the end of the transthoracic, epicardial, ventricular lead. This would cause lead V_3 to function as a unipolar epicardial wire. This postulate has subsequently been tested in another patient with temporary transthoracic ventricular epicardial leads after a cardiac operation. A similar pattern of ST elevation was noted in lead V_3 when contact was made with the pacemaker lead. There was no change in the other 11 leads of the cardiogram.

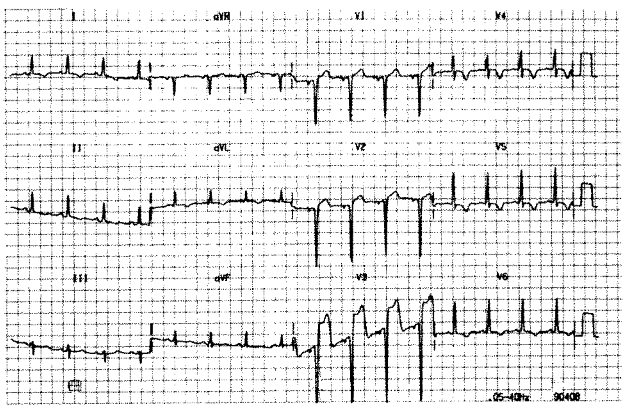

Fig 1. Twelve-lead electrocardiogram showing marked ST elevation in V_3 on the fourth postoperative day.

When transthoracic pacemaker leads are not in use, care should be taken to assure that they are electrically isolated. Failure to assure electrical isolation might result in dangerous complications. Less seriously, an isolated "current of injury" may be seen on the electrocardiogram causing an incorrect diagnosis. The fact that this change occurs in only one lead should alert the clinician to the possibility of this phenomenon.

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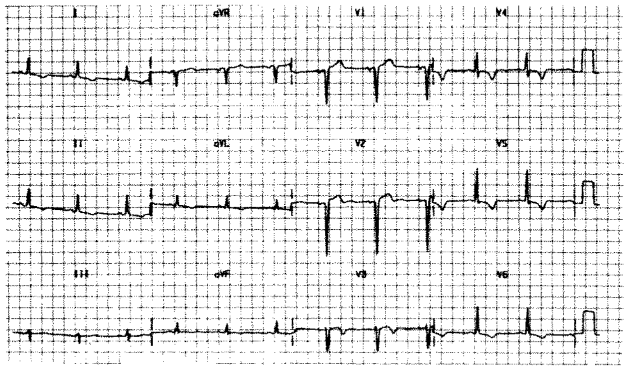

Fig 2. Electrocardiogram from the fifth postoperative day. (This tracing is identical to that of the third postoperative day.) There is evidence of remote anteroseptal infarction with slight ST elevation in V_1 through V_3.

Twenty-seventh Annual Meeting The Society of Thoracic Surgeons

The Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons was held at the Moscone Convention Center in San Francisco on February 18–20, 1991, with an attendance of 2,258 registrants, including spouses and exhibitors. The Scientific Sessions were attended by 679 members, 60 Candidate members, and 412 guests, including 156 residents.

Six hundred forty-three registrants were present at the Twenty-fourth Annual Postgraduate Course. At the Postgraduate luncheon, Dr Jack M. Matloff spoke on "Future Directions in Cardiovascular Healthcare." Co-Chairmen Drs Kent W. Jones and Andrew S. Wechsler and the members of the Committee on Postgraduate Education are to be commended for putting together an excellent program.

Breakfast Sessions were held on two mornings. Attendance at each was limited to ensure informality and encourage member participation. The first Breakfast Session was devoted to case presentations of difficult problems and the second to small clinical workshops on selected topics. The success of these sessions and the scientific program was due chiefly to the substantial effort of the Program Committee under the vigorous leadership of Drs Alexander S. Geha and Robert A. Guyton.

W. Gerald Rainer's Presidential Address was entitled "Profiles of Leadership in Thoracic Surgery." It will appear in the June issue of *The Annals*. The J. Maxwell Chamberlain Memorial Paper, "The Role of Staging in Prognosis and Management of Thymoma," was presented by Dr Earle W. Wilkins. His co-authors were Drs Hermes C. Grillo, J. Gordon Scannell, Ashby C. Moncure, and Douglas J. Mathisen. The First Ralph D. Alley Lecture, entitled "The Future of American Thoracic Surgery," was delivered by Harry Schwartz, PhD, columnist for *The American Medical News*.

Dr Daniel J. Ullyot chaired the Local Arrangements Committee. Mrs Robert W. Jamplis (Bobby) headed the Spouses Hospitality Committee. Mrs Jamplis and all spouses serving on the committee provided an array of excellent tours and a warm and gracious spouses' hospitality area. The Annual Reception was attended by 580 members and guests at the Palace of the Legion of Honor. Dr Ullyot and Mrs Jamplis and their committees did an outstanding job in creating an interesting and smoothly run program.

The Seventh Spouses Postgraduate Program was organized by Mrs Harold C. Urschel, Jr (Betsey). The attendance at this innovative program, "Love, Anger, and Relationships," was 85.

At the Annual Business Meeting, the following officers were elected: Robert W. Jamplis, *President*; Vincent L. Gott, *Vice President*; Richard P. Anderson, *Secretary*; Robert L. Replogle, *Treasurer*; Nicholas T. Kouchoukos, *Treasurer-Elect*; and Robert G. Ellison, *Historian*. Leonard L. Bailey and Peter C. Pairolero were elected *Councillors at Large*. Thomas B. Ferguson continues as *Editor* of *The Annals of Thoracic Surgery*. A complete list of the officers, committee members, and society representatives follows this report. The Society extends its appreciation to retiring officers and committee members for their dedicated service.

Three hundred twenty-eight members were elected. These new members increased the total membership to 3,111.

The Smith Bucklin staff are to be commended for their hard work and diligence, which produced an outstanding meeting.

The next meeting of The Society will be the Second International Conference on Circulatory Support Devices in End-Stage Heart Disease in San Francisco, California, on November 15–17, 1991. The Twenty-eighth Annual Meeting will be held February 3–5, 1992, in Orlando, Florida.

Richard P. Anderson, MD
Secretary

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(Deadline: September 1, 1992)

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CALL FOR ABSTRACTS

(Deadline: September 9, 1991)

Abstracts for papers to be presented at the 1992 Annual Meeting are now being accepted. The deadline for receipt of abstracts is September 9, 1991. No papers *received* after this date will be accepted for inclusion in this year's program. An original and one copy should be submitted, using the official Society abstract form (on verso of this page), to Delos M. Cosgrove III, MD, and Douglas J. Mathisen, MD, Co-Chairmen, Program Committee (Abstracts), The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611. Additional forms are available upon request from The Society. Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. Abstracts must be in the hands of the Program Committee by **September 9, 1991.** Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

The Thoracic Surgery Directors Association (TSDA) has established a Resident Presentation Award. Potential TSDA Resident Award abstracts must represent original work by the resident, who is to be first author and presenter. TSDA Resident Award abstracts may be directed to the regular Scientific Session or the Research Forum.

Essayists are reminded that according to the bylaws of The Society, all papers accepted for presentation: (1) must be submitted in *triplicate* to the Secretary at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation; and (2) become the property of The Society if they are accepted for presentation.

It is well recognized that abstracts frequently belie their content by virtue of poor organization, and as a result valuable contributions to the Scientific Sessions may be unrecognized. It is important that methods and results be clearly defined in the abstract; therefore, general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Speakers for accepted papers are limited to ten minutes.

Instructions for Abstracts

The official abstract form printed on verso of this page and available from The Society, or photocopies thereof, must be used. **Authors must categorize the principal subject of their abstract by checking the appropriate box.**

If the author wishes to submit the abstract for consideration for the Thoracic Surgery Directors Association Award competition, the *additional* appropriate box must be checked. Also, the name of the Program Director must appear on a TSDA Resident Award abstract.

1. Full names of authors must appear on the abstract.
2. Institution or address is to be given, but omit titles, degrees, and appointments.
3. Abstracts must be limited to 250 words and must be typed double-spaced.
4. When percentages are used, the absolute numbers of derivation must be stated.
5. The body of the abstract should include:
   a. A brief statement of the purpose of the study being presented, with reference to the current state of research in the field.
   b. The methods of study or experimental approach clearly, but briefly, defined.
   c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
   d. A statement concerning the significance of the work and its possible implications for further research.
6. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

In discussion of papers, The Society encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of discussion in the form of "secondary papers" will not be welcomed.

CALL FOR SURGICAL FILMS OR VIDEO TAPES

(Deadline: August 27, 1991)

The popular Surgical Motion Picture program will again be presented at the Orlando meeting. The Program Committee hereby solicits the submission of surgical audiovisual presentations, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to The Society. The film (tape) may not exceed ten minutes in length. Sound is acceptable but not necessary; however, live narration by the principal surgeon is a requirement for participation in the movie night program. Presentations should be on 16-mm film, ¾-inch U-Matic video tape, or ½-inch VHS tape. The deadline for submission is **August 27, 1991.** Films and video tapes also should be sent to Delos M. Cosgrove III, MD, and Douglas J. Mathisen MD, Co-Chairmen, Program Committee, at The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611.

Richard P. Anderson, MD
Secretary

For Committee use only:

THE SOCIETY OF THORACIC SURGEONS

Abstract Form

LIMIT TO 250 WORDS AND DOUBLE-SPACE

For Committee use only:
Rating: (Highest 1)

1☐ 2☐ 3☐ 4☐ 5☐

TITLE

AUTHOR(S)

ADDRESS

PLEASE CHECK ONE APPROPRIATE CATEGORY

- ☐ **Pulmonary**
- ☐ **Esophagus**
- ☐ **Chest wall Mediastinum**
- ☐ **Trauma**
- ☐ **Transplantation**
- ☐ **Heart**
- ☐ **Great vessels**
- ☐ **Valves**
- ☐ **Congenital**
- ☐ **Coronary**
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- ☐ **Myocardial protection**
- ☐ **Extracorporeal circulation**
- ☐ **Endoscopy**
- ☐ **Vascular surgery**
- ☐ **Research, Cardiac**
- ☐ **Research, Congenital Cardiac**
- ☐ **Research, Transplantation**
- ☐ **Research, General Thoracic**

☐ PLEASE CHECK IF ALSO SUBMITTED FOR THE THORACIC SURGERY DIRECTORS ASSOCIATION AWARD

Program Director's Name:

I acknowledge that the material will not be presented elsewhere if accepted for presentation on The Society of Thoracic Surgeons Scientific Program. I further understand that the Editorial Board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

Signature of Senior Author

Information About Membership in The Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) is the largest organization devoted primarily to the practice of thoracic and cardiovascular surgery. The major purpose of The Society is educational, with the aim of providing thoracic and cardiovascular surgeons from both academic and private practice environments a forum for presentation and discussion of scientific topics. As outlined in the original bylaws of The Society, this educational emphasis is designed to accomplish the broader goal of improving the quality and practice of thoracic and cardiovascular surgery as a specialty.

The STS recently held its 27th Annual Meeting. Since its founding in 1964, The Society has grown continually; the membership now includes the majority of board certified thoracic surgeons in the United States as well as thoracic and cardiovascular surgeons from 45 other countries.

In addition to holding an annual scientific meeting, the STS has more than 20 committees working on diverse matters related to improving thoracic and cardiovascular surgery as a specialty. Examples of these committees are: Standards and Ethics, Government Relations, Medico-Legal Affairs, Surgical Standby for PTCA, Nomenclature and Coding, Education and Resources, and Cardiothoracic Surgical Practice Guidelines. The Committee to Analyze Circulatory Assist Devices and Artificial Hearts sponsors topical meetings (next meeting, November 15–17, 1991, in San Francisco). The Committee to Develop a National Database for Thoracic Surgery has implemented the first comprehensive database program for thoracic and cardiovascular surgeons in the United States; it is currently being offered to Society members.

There are five types of membership in The Society of Thoracic Surgeons: active, senior, honorary, international, and candidate.

Active Member Applicants for active membership must be surgeons whose practice is devoted primarily to the field of thoracic and cardiovascular surgery.

QUALIFICATIONS: Applicants must be Diplomates of the American Board of Thoracic Surgery or Fellows in The Royal College of Surgeons of Canada, and be established in the practice of thoracic and/or cardiovascular surgery for a minimum of 3 years. There must be sponsoring letters from three active STS members.

Senior Member Any active member or international member, upon reaching the age of 65 years, shall automatically become a Senior Member.

Honorary Member Honorary membership shall be reserved for distinguished persons worldwide who have achieved prominence in the field of thoracic and cardiovascular surgery and have contributed to its advancement. Honorary members shall be elected by a majority vote of The Society at its annual business session upon recommendation of the Council of the STS.

International Member Members from countries other than the United States and Canada were previously accepted only as active members. Because of differences in training and practice, the application process for foreign members was often complex and time consuming. To allow for greater international participation, the bylaws were revised to provide for the category of international member.

QUALIFICATIONS: Applicants shall reside outside the United States and Canada. They shall have completed training equivalent to that required for active membership. They shall have achieved appropriate certification or recognition of achievement in the specialty in their country and must devote the majority of their professional efforts to the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee.

Candidate Member The candidate membership category was created to allow participation of younger surgeons not yet qualified for active membership.

QUALIFICATIONS: Applicants shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a training program similarly approved by The Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in process of acquiring certification or have been certified by the American Board of Thoracic Surgery or The Royal College of Surgeons of Canada and are awaiting fulfillment of the 3-year residence requirement for active membership are eligible for this type of membership.

If you would like to receive an application for membership in The Society, send the request printed below. This year's deadline for receipt of applications is September 1, 1991. We suggest you apply soon as it takes time to process the application. Approved applications will be presented to the membership at the February 1992 Annual Meeting in Orlando, FL.

REQUEST FOR APPLICATIONS

Please send an application for: ☐ Active membership ☐ International membership ☐ Candidate membership

TO: NAME: ____________________

ADDRESS: ____________________

____

TELEPHONE NUMBER: ____________________

Send to: James L. Cox, MD, Chairman, Membership Committee
The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611
Telephone: (312) 644-6610; FAX: (312) 527-6635

THE
ANNALS OF
THORACIC
SURGERY

*Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association*

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

The International Society for Cardiovascular Surgery/The Society for Vascular Surgery, Boston, Massachusetts—June 3–5, 1991

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Warm Heart Surgery: Theory, Concepts and Practice, Toronto, Ontario, Canada—June 20, 1991

For information on this meeting, contact Continuing Education, Faculty of Medicine, University of Toronto, Medical Sciences Building, Toronto, Ont M58 1A8, Canada; or telephone (416) 978-2718.

Seventeenth Annual Meeting of The Western Thoracic Surgical Association, Seattle, Washington—June 26–29, 1991

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Second International Seminar on Transplantation for End-Stage Lung Disease, Zurich, Switzerland—June 27–28, 1991

For information on this meeting, contact A.K.M. Congress Service, Clarastrasse 57, Ch 4005 Basel, Switzerland; or telephone 061-691-8888 (facsimile: 061-691-8189).

Techniques in Pulmonary and Oesophageal Surgery, Liverpool, England—July 14–16, 1991

For information on this meeting, contact Mr R. J. Donnelly, The Cardiothoracic Centre, Broadgreen Hospital, Thomas Dr, Liverpool L14 3LB, England; or telephone 051 228 4878 (facsimile: 051 220 8573).

Twentieth World Congress of The International Society for Cardiovascular Surgery, Amsterdam, the Netherlands—September 1–6, 1991

For information on this meeting, contact the Registrar: XX World Congress—ISCVS, International Travel Service, Inc, 104 Wilmot Rd, Suite 300, PO Box 825, Deerfield, IL 60015; or telephone (708) 940-2100 (facsimile: (708) 940-2386); or contact the Congress Secretariat, International Society for Cardiovascular Surgery, 13 Elm St, Manchester, MA 01944: or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Current Issues in Thoracic Organ Transplantation, Essen, Germany—September 19–21, 1991

For information on this meeting, contact Organizing Secretariat, Gisa Brodde Meetings, Saalbau Essen, PO Box 100301, D-4300 Essen 1, Germany; or telephone (0)201-232121 (facsimile: (0)201-232273).

Heart Valve Replacement—Past Performance: Future Prospects, Sheffield, United Kingdom—September 19–21, 1991

For information on this meeting, contact Jenny Pupius, Symposium Secretariat, Department of Medical Physics and Clinical Engineering, Royal Hallamshire Hospital, Glossop Rd, Sheffield S10 2JF, United Kingdom; or telephone (0742) 555250 (facsimile: (0742) 729981).

Fifth Annual Meeting, European Association for Cardio-Thoracic Surgery, London, United Kingdom—September 22–25, 1991

For information on this meeting, contact Organising Secretariat, Conference Associates & Services, Ltd, Congress House, 55 New Cavendish St, London W1M 7RE United

Kingdom; or telephone 071 486 0531 (facsimile: 071 935 7559; telex: 934 346 CONFAS G).

Fifth Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery, Alexandria, Egypt—September 23–27, 1991

For information on this meeting, contact Prof M. El-Fiky, Chairman, Cardiac Surgery Department, Ain Shams Faculty of Medicine, Abbassia, Cairo, Egypt; or telephone (202) 834981 or (202) 835495 (facsimile: (202) 834981).

Arterial Grafts for Coronary Bypass Surgery, Brussels, Belgium—September 29–October 2, 1991

For information on this workshop, contact R. Dion, MD, Cliniques Universitaires St. Luc, Chirurgie Cardiaque, ave Hippocrate, 10, B 1200 Brussels, Belgium; or telephone 32/2/764.61.06 or 764.61.07 (facsimile: 32/2/764.37.03).

Mitral Surgery Advances and Controversies, Varese, Italy—October 4–5, 1991

For information on this meeting, contact Erreci Congressi sri, Via Negroni, 4/7, 28100 Novara, Italy; or telephone 0321-393021 or 398977 (facsimile: 0321-393026).

American College of Surgeons, Chicago, Illinois—October 20–25, 1991

For information on this meeting, contact American College of Surgeons, 55 Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-seventh Annual Scientific Assembly, American College of Chest Physicians, San Francisco, California—November 4–8, 1991

For information on this meeting, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, Florida—November 7–9, 1991

For information on this meeting, contact Hendrick B. Barner, MD, Southern Thoracic Surgical Association, 401 N Michigan Ave, Chicago, IL 60611-4267; or telephone (312) 644-6610 (facsimile: (312) 321-6869).

Third Combined Meeting of the Nederlandse Vereniging Voor Thoraxchirurgie and the Deutsche Gesellschaft für Thorax-, Herz- und Gefäßchirurgie, Maastricht, the Netherlands—November 7–9, 1991

For information on this meeting, contact Organizing Secretariat, Conference Agency Limburg, Mrs Brigitte Bessems, c/o University Hospital Maastricht, PO Box 1918, 6201 BX Maastricht, the Netherlands; or telephone 31 (0)43 258344 (facsimile: 31 (0)43 258355).

Sixth World Conference on Lung Cancer, Melbourne, Australia—November 10–14, 1991

For information on this meeting, contact Ms Jane Willis, MCS Convention Services, PO Box 335, Heidelberg, Vic 3079, Australia; or telephone (613) 499-6722 (facsimile: (613) 499-7137).

Sixty-fourth Scientific Session of the American Heart Association, Anaheim, California—November 11–14, 1991

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 750-5300.

Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, Florida—February 3–5, 1992

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

CLASSIFIED ADS

Classified ads for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Arthur Carlucci, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010 (telephone: (212) 633-3806; facsimile: (212) 633-3880). All ads are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.25 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $17.00 per insertion for box number ads.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Ad orders should be for a maximum of 6 months; ads may be renewed for up to 6 months at a time. Ad copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Ads, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3853). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the ad. To respond to an anonymous ad, write to Box Number, *The Annals of Thoracic Surgery*, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Thoracic/vascular surgeon needed to join prominent, active 3-man group in desirable suburban community in greater NY metropolitan area. Excellent opportunity for well-trained, highly motivated individual. Recent graduate preferred. Possible academic affiliation. Please respond with CV.

Please respond to Box 404. 404D/I

Minneapolis cardiothoracic/vascular group seeks to add fifth surgeon, BC/BE.

Respond to BLH Physician Search, 2231 Lee Ave N, Minneapolis, MN 55422; (612) 588-1116 or -0333. 438L/E

Board certified/eligible cardiothoracic surgeon for busy 1-physician practice in Atlanta. Transplant experience. Future partnership.

Send resume to Georgia Cardiac Surgical Association, PO Box 491203, College Park, GA 30349. 439L/E

Cardiovascular and thoracic surgeon, BE/BC, to join another physician in a rapidly expanding private practice located in the Southeast. Please send curriculum vitae and references.

Please respond to Box 459. 459L/E

University of Massachusetts Medical Center is recruiting candidates for its newly opened Cardiothoracic Surgical Residency Program for 1991, 1992, and 1993. The applications for the 1993 position will be processed through the Match Program for Cardiothoracic Residencies.

Request applications from and submit curriculum vitae and three letters of recommendation to Thomas J. Vander Salm, MD, Chief, Division of Cardiothoracic Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655; telephone: (508) 856-2216. 462L/E

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in Dallas. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Respond to Practice Enhancement Resources, PO Box 655999, Dallas, TX 75265; Attention: Carol. 487B/F

Cardiovascular and thoracic surgeon to join established 3-man private practice in mid-South. Practice includes thoracic, cardiac, and vascular surgery. Must be board certified or eligible in thoracic and cardiovascular surgery. Prefer candidate who has recently completed his/her training. Please respond with curriculum vitae.

Please respond to Box 489. 489B/G

Cardiothoracic surgeon, BE/BC, wanted to join 2 surgeons in busy and expanding practice on the West Coast. Experience or training in adult cardiac surgery, thoracic surgery, pacemaker surgery, valve repair, and arrhythmia surgery necessary. Position available July 1991; new or recent graduate preferred. Excellent salary and benefits with eventual partnership possible. Send curriculum vitae and references.

Please respond to Box 497. 497C/E

Clinical associate: a very busy adult cardiac surgery practice located in northeast Philadelphia is seeking an ABTS eligible or certified clinical associate.

Submit inquiries and CV to John Bell-Thomson, MD, Chairman, Division of Cardiothoracic Surgery, Albert Einstein Medical Center, 5501 Old York Rd, Philadelphia, PA 19141. 501E

Cardiovascular surgeon wanted to join a 2-man group in an established practice in the Southeast. Would prefer a recent graduate, but all applications considered. Generous salary leading to partnership. Practice includes all aspects of adult cardiac, thoracic, and vascular surgery. Send curriculum vitae with experience and recommendations.

Please respond to Box 502. 502C/E

Cardiothoracic surgeon to join group of two, in Michigan. Please respond with CV and references.

Please respond to Box 504. 504C/H

Cardiac surgeon with 3 to 5 years experience in adult cardiac surgery wanted for immediate opening in Northeast. Program now doing 30 to 40 cases/month and senior surgeon needs an experienced #2 individual for long-term commitment. Excellent salary leading to partnership. Reply with curriculum vitae.

Please respond to Box 508. 508C/E

Cardiovascular and thoracic surgeon, board eligible or certified, wanted to join another surgeon in private practice in the Southeast. Please respond with curriculum vitae.

Please respond to Box 509. 509C/H

General thoracic surgeon: the Department of Surgery and the Section of Thoracic Surgery invite applications and nominations for a faculty position in general thoracic surgery at the Assistant or Associate Professor level at the University of Chicago. Prospective candidates should be American Board of Thoracic Surgery eligible or qualified as of July 1, 1991, have demonstrated excellence in clinical surgery and research, and possess a commitment to teaching. Preference will be given to those who have broad experience in general thoracic surgery, including lung transplantation. The successful candidate is expected to develop his/her own research program.

Applicants should have their curriculum vitae and two letters of recommendation sent to Dr Mark Ferguson, Chief, Section of Thoracic Surgery, The University of Chicago, Box 255, 5841 Maryland, Chicago, IL 60637; facsimile: (312) 702-5909. Applications must be received by June 1, 1991. The University of Chicago and its Medical Center are affirmative action/equal opportunity employers. 510C/E

Cardiovascular surgeon to join a young diplomate, ABTS, in a practice that has grown to some 600 hospital surgeries per year. Location is in a city in the mid-South. The only open heart program in 15 counties. 325-bed regional medical center, 2 catherization labs. Practice consists of cardiac, thoracic, and vascular surgery. Full financial support including productivity incentive. All benefits, malpractice and office expenses provided.

Please respond to Box 511. 511C/E

Cardiovascular surgeon: we are looking for a recently trained B/E or B/C CV surgeon to join our very busy and enjoyable 2-man Cardiovascular Department at Billings Clinic, a progressive major regional multispecialty clinic in the northern Rocky Mountain region. This is an outstanding practice opportunity for the right individual seeking a challenging and rewarding surgical practice in surroundings conducive to the highest quality of living for the surgeon and his or her family.

For further information, please call (406) 256-4766 or forward CV to Ann B. Oglesby, MD, MDA, Medical Director, Billings Clinic, PO Box 35100, Billings, MT 59107-5100. 512C/E

Academic cardiothoracic surgeon: the Division of Cardiothoracic Surgery at the University of Massachusetts is expanding its academic faculty. Candidates will be expected to have an interest in developing an active cardiothoracic practice, to participate in thoracic and general surgical residency training, and to take part in clinical and/or laboratory research. The University of Massachusetts is an equal opportunity employer.

Please respond with curriculum vitae to Thomas J. Vander Salm, MD, University of Massachusetts Medical Center, 55 Lake Ave, North, Worcester, MA 01655. 516C/E

Cardiovascular and thoracic surgeon, BC/BE, recently trained, to join an established 3-man private practice group in Southeastern coastal capital city and two-university town. Great hunting, fishing, and sports. Submit CV and references.

Please respond to Box 519. 519D/I

Cardiac surgeon, ABTS eligible/certified. Position available immediately to join established 4-surgeon group practicing adult cardiac surgery. Excellent opportunity for new or recent grad. Practice located in Reading, PA (southeast PA within easy distance of New York and Philadelphia). Guaranteed starting salary and excellent benefits.

Send CV and references to Ashworth and Gregory MDs, 1235 Penn Ave, Wyomissing, PA 19610; (215) 374-5000. 520D/F

Pediatric cardiac surgeon to assume responsibility for established (120 cases per year) and growing pediatric cardiac program as of July 1, 1991.

Address correspondence to Neil R. Thomford, MD, Professor and Chairman, Department of Surgery, Medical College of Ohio, PO Box 10008, Toledo, OH 43699-0008. 522D/G

Noncardiac thoracic surgeon—due to retirement, The Mary Imogene Bassett Hospital is seeking a general/thoracic surgeon. MIBH is a multispecialty group practice with a surgical residency and research opportunities. Excellent lifestyle and recreation. Academic appointment at Columbia University.

Contact Michael S. Gold, MD, Surgeon-in-Chief, One Atwell Rd, Cooperstown, NY 13326; (607) 547-3968. 525D/E

Assistant surgeon sought for busy adult cardiothoracic surgery practice. Entire responsibility will be to assist four senior surgeons in the operating room. Board certification or eligibility in general surgery, and some experience in vascular and/or thoracic surgery, desirable. Must be licensed in Pennsylvania or able to obtain license. Generous salary and fringes. Position is available immediately and could be permanent. Ideal location in very pleasant, small city near major eastern metropolitan centers.

Please respond with CV to Lawrence I. Bonchek, MD, 555 N Duke St, Lancaster, PA 17603; (717) 295-8395. 527E/F

Cardiothoracic surgeon—board certified/eligible and recently trained, to join an established and expanding private practice of cardiac surgery.

Please respond with curriculum vitae and details of experience to John M. Postel, MD, Chief of Cardiac Surgery, Cedars Medical Center, 1400 NW 12th Ave, Miami, FL 33136. 528E

Cardiothoracic/vascular surgeon, BE/BC, wanted to join growing practice in New Jersey. Recent graduate preferred. Please respond with CV.

Please respond to Box 529. 529E/G

Director, cardiac transplant program—The Department of Surgery, Medical College of Ohio, is seeking a board certified or board eligible cardiothoracic surgeon to direct established heart transplant program.

Curriculum vitae and bibliography should be submitted to Neil R. Thomford, MD, Chairman, Department of Surgery, PO Box 10008, Toledo, OH 43699-0008. The Medical College of Ohio is an equal opportunity employer. 530E/G

Thoracic surgeon wanted: a busy general thoracic surgical practice (non–open-heart, nonvascular) 20 miles south of Boston seeks to add a third surgeon. Candidate must be board certified or eligible. This active practice operates from a multihospital referral base. The community is an ideal area for family living, with excellent schools and nearby Boston and Cape Cod cultural and recreational facilities. Competitive salary, malpractice insurance, and excellent benefits package. Please respond with CV.

Please respond to Box 531. 531E/J

Thoracic/vascular surgery practice available. Established practice including noninvasive vascular lab in metropolitan Washington, DC. Physician planning to retire after 35 years. Will stay on to assure smooth transition and continuity of practice referrals.

Interested parties should send CV and letter of intent to Richard F. Cioffi, MD, Vice President, Medical Affairs, Holy Cross Hospital, 1500 Forest Glen Rd, Silver Spring, MD 20910. 532E/F

Cardiothoracic surgeon needed for rapidly expanding program located in a coastal area of the Southeast. Private practice, primarily adult cardiac and thoracic. BC/BE required. Respond with curriculum vitae and names of references.

Please respond to Box 533. 533E/J

Associate director for heart transplantation is urgently needed for rapidly expanding heart transplantation program in California. Excellent benefits package. Please respond with curriculum vitae and outline of surgical experience.

Please respond to Box 534. 534E/J

Cardiovascular and thoracic surgeon: excellent opportunity for a board certified/eligible cardiovascular and thoracic surgeon to join a large cardiac surgery group in southern California. Must have a minimum of 1 year experience in pediatric and neonate cardiac surgery (including fellowship). Excellent fringe benefits.

Please reply with curriculum vitae and outline of surgical experience.

Please respond to Box 535. 535E/J

Cardiothoracic surgeon needed for established cardiac program in the Philadelphia area. Must be BE/BC. New or recent graduate preferred. Salary leading to partnership.

Please send CV to Ms Rosemary Morrone, Administrator, Department of Surgery, 3 Cooper Plaza, Suite 411, Camden, NJ 08103. 536E/F

Thoracic and vascular surgeon, board certified, to join active (noncardiac) thoracic and vascular practice in northern New Jersey. Competitive salary and benefits. Please respond with curriculum vitae.

Please respond to Box 537. 537E/G

Thoracic-vascular surgeon: excellent opportunity for well-trained board certified surgeon to join and eventually buy well-established solo practice with university-affiliated hospital in large eastern city. Please submit CV.

Please respond to Box 539. 539E/G

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 398. 398C/H

SITUATIONS WANTED

General thoracic surgeon, 36, Canadian fellowship including training in UK. Special interest in esophageal including motility and 24-hour pH. Four years in private practice. Interested in group, academic, and/or private practice. CV and references upon request.

Please respond to Box 521. 521D/F

FELLOWSHIPS

Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite 312, Sacramento, CA 95819. 480A/L

A 2-year Cardiovascular Research Fellowship position is available 7/1/91 in the Division of Cardiothoracic Surgery at the University of Massachusetts Medical Center. This is an opportunity for a closely supervised and highly productive cardiac research experience. Requirements: (1) A minimum of 2 years of surgical training; (2) a commitment from an institution to complete the applicant's training in general surgery; (3) intentions to pursue an academic career in cardiothoracic surgery.

Interested candidates should contact Marc S. Visner, MD, Division of Cardiothoracic Surgery, University of Massachusetts Medical Center, 55 Lake Ave North, Worcester, MA 01655; telephone: (508) 856-2975. 461L/E

Fellowship in cardiovascular surgery available July 1, 1991. High-volume program with outstanding Fellow involvement and training. Excellent salary and benefits. American Board of Surgery eligibility required.

Please contact M. Terry McEnany, MD, Kaiser Foundation Hospital, 2350 Geary Blvd. San Francisco, CA 94115; (415) 929-5499. 513C/H

Fellowship in cardiothoracic and vascular surgery available July 1, 1991. Program includes over 400 open heart surgery cases and 200 thoracic or vascular procedures. New Jersey medical license required. Good salary and benefits.

Please contact Arthur J. Roberts, MD, Director, Jersey Shore Heart Institute, PO Box 1143, Neptune, NJ 07753. 514C/E

Fellowship in thoracic and cardiovascular surgery available July 1, 1991. Good salary. Research opportunities.

Please send inquiries to George C. Morris, Jr, MD, and Gerald M. Lawrie, MD, Baylor College of Medicine, Houston, TX 77030; (713) 797-9428. 538E/G

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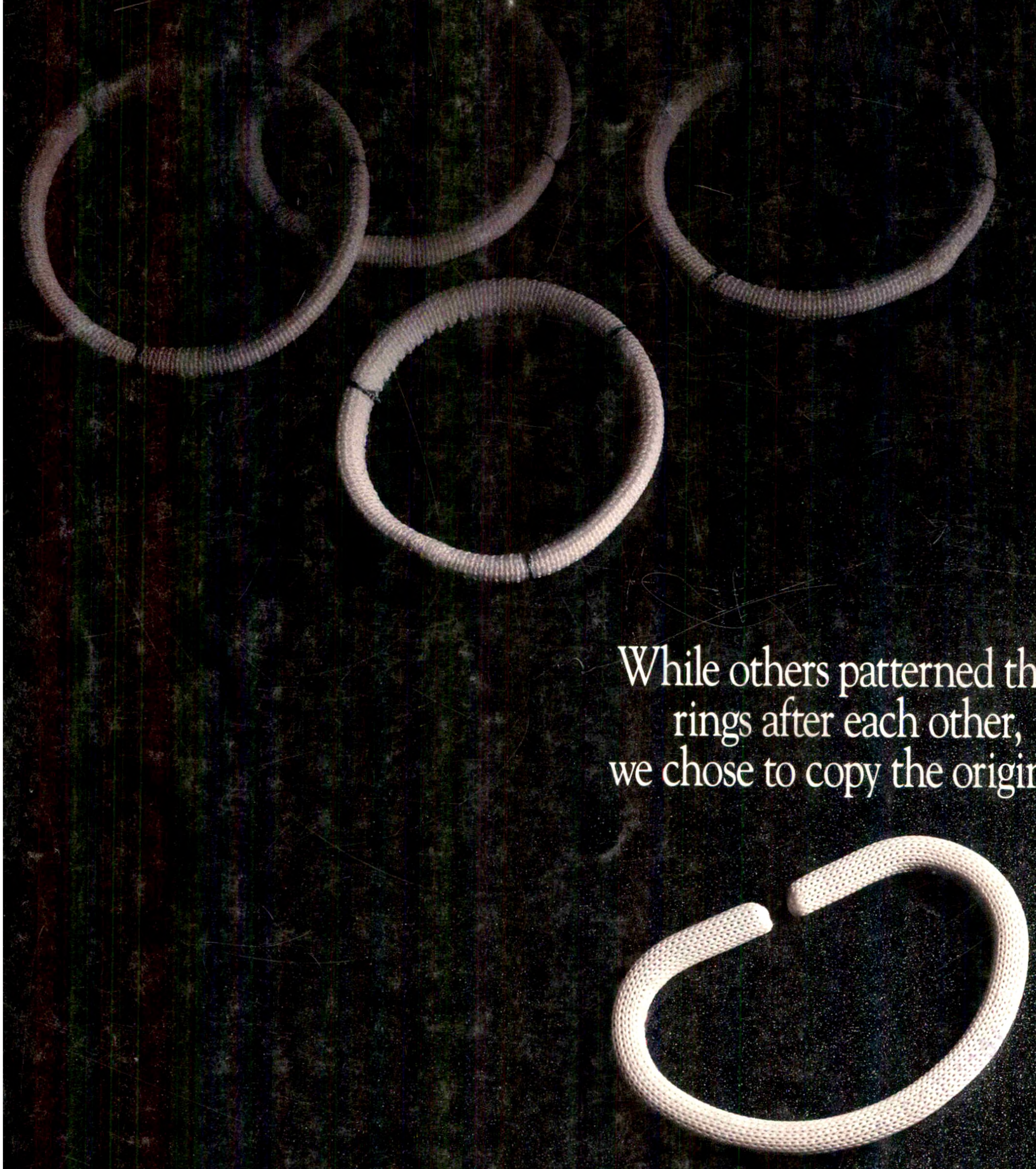
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THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons
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Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association
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Circulatory Support 1991, November 15–17, 1991
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Indications: Bioprostheses are indicated for use in patients suffering from valvular heart disease. Aortic and mitral valvular heart disease are conditions involving any of the following: obstructions of the heart valves, or stenosis; leakage of the valves, known as regurgitation or insufficiency; and combinations of the two, sometimes referred to as mixed disease or combined lesions. Valvular heart disease may be caused by any number of factors, including congenital abnormalities, infection by various microorganisms, degenerative calcification, rheumatic heart disease and rupture or dysfunction of the mitral subvalvular mechanism secondary to myocardial ischemia. Bioprostheses are used particularly in those patients for whom long-term anticoagulation is contraindicated or who may be difficult to maintain on anticoagulation therapy. The Carpentier-Edwards bioprosthesis is intended for use in patients whose aortic or mitral valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic or mitral valve prosthesis which is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. **Warnings:** For Single Patient Use Only In the presence of conditions affecting calcium metabolism or when calcium-containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients under 20 years of age, in patients on a high calcium diet, in the presence of severe systemic hypertension, and in patients who are on maintenance hemodialysis. The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient are made, and alternative methods of treatment are considered. Overall durability, especially long-term, has not been established for bioprostheses. Serious complications, sometimes leading to replacement of the valve and/or death, may be associated with the use of prosthetic valves (see Complications). A full explanation of the benefits and risks should be given to each prospective patient before surgery. **Note:** Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis. Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection. Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy, except where contraindicated, during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall or history of previous atrial thrombosis. The appropriate anticoagulation therapy must be determined by the physician on an individual basis. **Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc. should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result. The Carpentier-Edwards bioprostheses must be kept moist at all times. Drying out will cause irreversible damage to the leaflet tissue. To prevent drying out during implantation, the valves should be irrigated periodically on both sides with sterile physiological saline.** Passing diagnostic catheters and transvenous pacing leads across a Carpentier-Edwards bioprosthesis could damage the valve. Consequently, it is recommended that these procedures be avoided. Both the valve and glutaraldehyde storage solution are **sterile.** The outside of the jar is **not sterile** and must **not** be placed in the sterile field. Furthermore, the valve and container should **never** be subjected to sterilization procedures involving ethylene oxide, propylene oxide, steam, or irradiation. Storage between 10°C and 25°C is recommended; however, care should be exercised to avoid freezing or extreme heat, which may damage the valvular tissue. **Any valve that has been frozen or exposed to temperatures greater than 60°C should not be used for human implantation.** Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat, and may also cause skin sensitization. Avoid prolonged or repeated contact or prolonged breathing of the vapor. Use only with adequate ventilation. In the event of contact, immediately flush the affected area with water. In the event of contact with eyes, seek medical attention. **Surgical Precautions: 1.** When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient. **2.** Due to the relative flexibility of the frame, care must be exercised to avoid the use of too large a prosthesis to prevent folding or extreme deformation of the stent that may render the valve incompetent. Oversizing may create highly localized mechanical stresses resulting in tissue failure in the form of detachment of the leaflets or porcine aortic wall from the valve stent posts. **3.** Left ventricular perforation or ulceration has been reported. Both open and closed chest cardiac massage in patients with an open strut mitral prosthesis increases the risk of ventricular perforation. Additionally, lifting, flexing, and manual compression of the distended heart after discontinuation of bypass may cause a commissure strut to be pushed through the endocardium, producing a dissecting hematoma with subsequent uncontrolled hemorrhage. **4.** The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or extreme distortion of the orifice. Edwards CVS Division has received reports in which individual mattress sutures, spanning a distance of 10 to 15mm, produced a purse-string effect causing compression of the valve orifice. **5.** When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures. **6.** Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue. **7.** As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised, particularly in mitral replacement, to avoid looping or catching a suture around the free legs which would interfere with proper valvular function. **8.** The stent of the bioprosthesis is asymmetrical to conform to the natural shape of the porcine aortic valve. Consequently, the commissure supports are not equidistantly spaced. The contrasting suture markers in the sewing ring of the mitral valve denote the greatest intercommissural distance. These two commissure supports should be oriented so as to straddle the ventricular outflow tract to avoid murmurs due to blood flow turbulence. **Note:** The contrasting suture material should not be removed from the prosthesis. **9.** In the aortic position, the struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia. **10.** A serial number tag is attached to the sewing ring of each valve by a suture. This serial number should be checked against the number on the jar; if any difference is noted, the valve should be returned unused. This tag should not be detached from the valve until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal. **11.** Gentle handling is required for all implantable devices. If the valve is dropped, damaged, or mishandled in any way, it must not be used for human implantation. **Complications:** As with all prosthetic heart valves, serious complications, sometimes leading to death, may be associated with the use of tissue valves. In addition, complications due to individual patient reaction to an implanted device, or to physical or chemical changes in the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device. Complications associated with the use of Carpentier-Edwards bioprostheses include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulant therapy, ventricular perforation by stent posts, looped sutures, and malfunctions of the valve due to distortion at implant or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, suture abrasion, instrument trauma, and leaflet or aortic wall detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarct. **Note:** Based on reports in the literature on tissue valves, there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes an apparent causal relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Carpentier-Edwards bioprostheses to calcification as compared to other commercially available porcine valves. **Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician. Baxter International Inc. is the owner of the following US patent which covers the products described herein: 4,106,129. Patent numbers in foreign countries supplied upon request. See package insert accompanying product for a full discussion of warnings, contraindications, complications and prescribing information. Carpentier-Edwards® is a registered trademark of Baxter International Inc.

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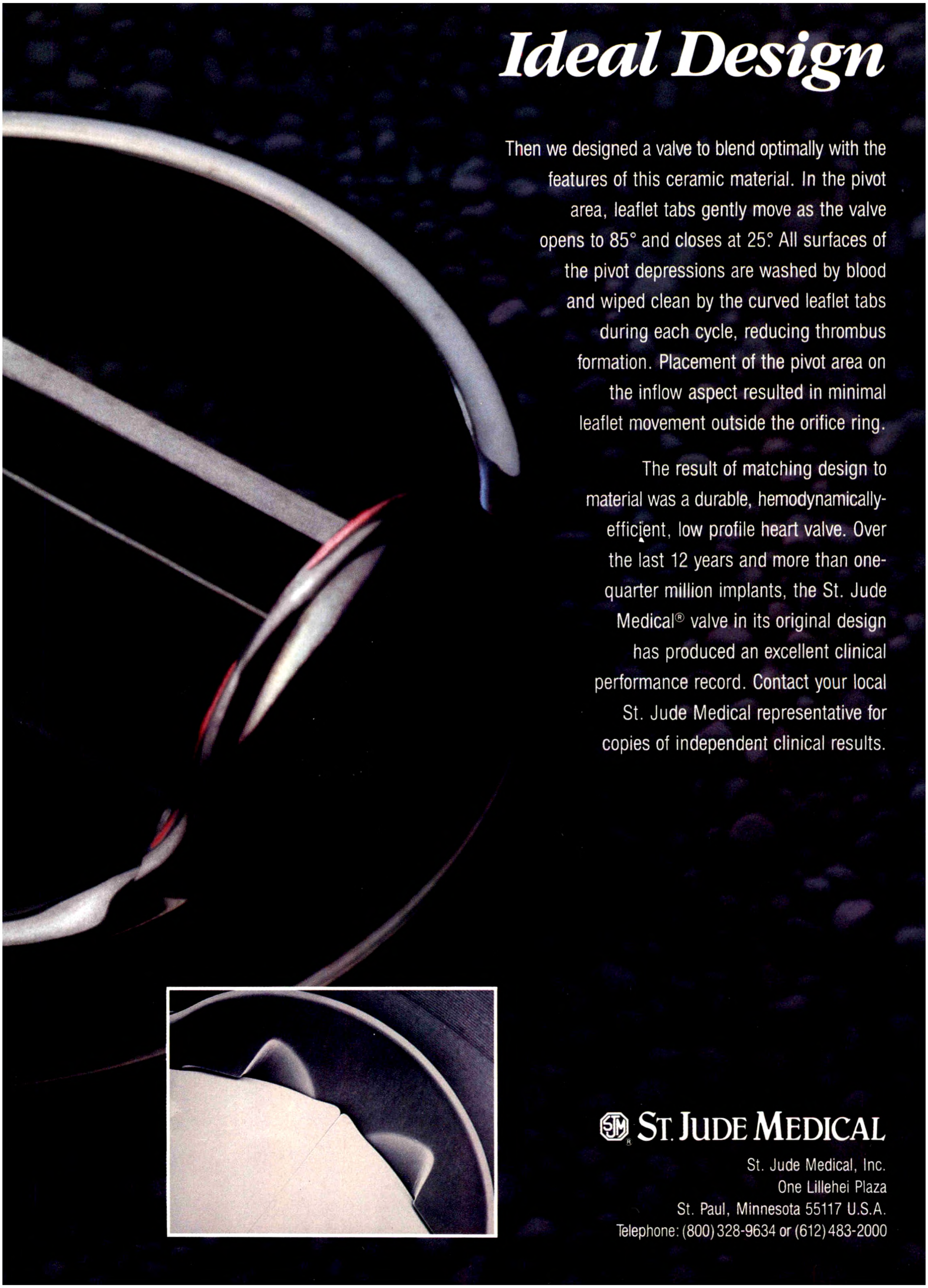

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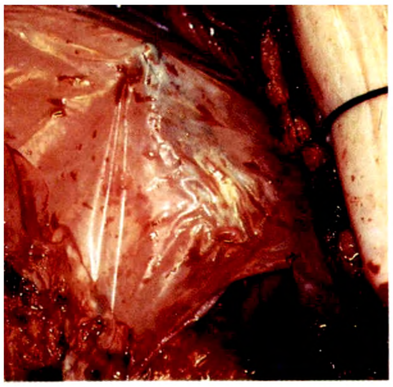

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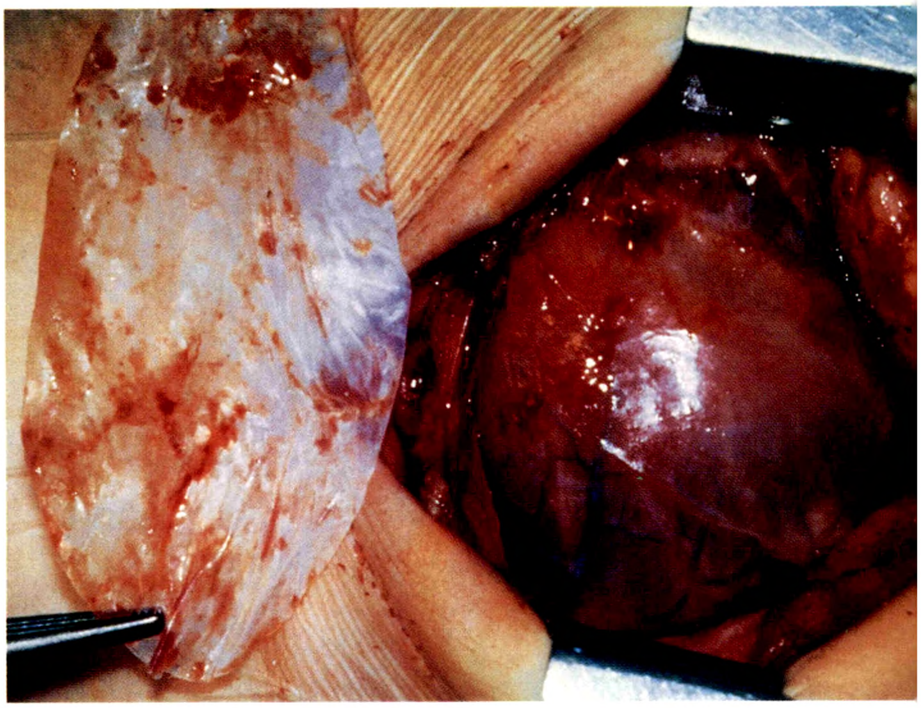

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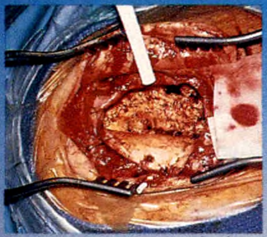

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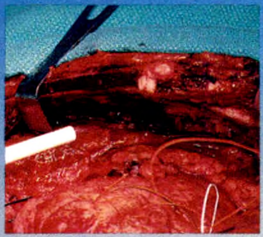

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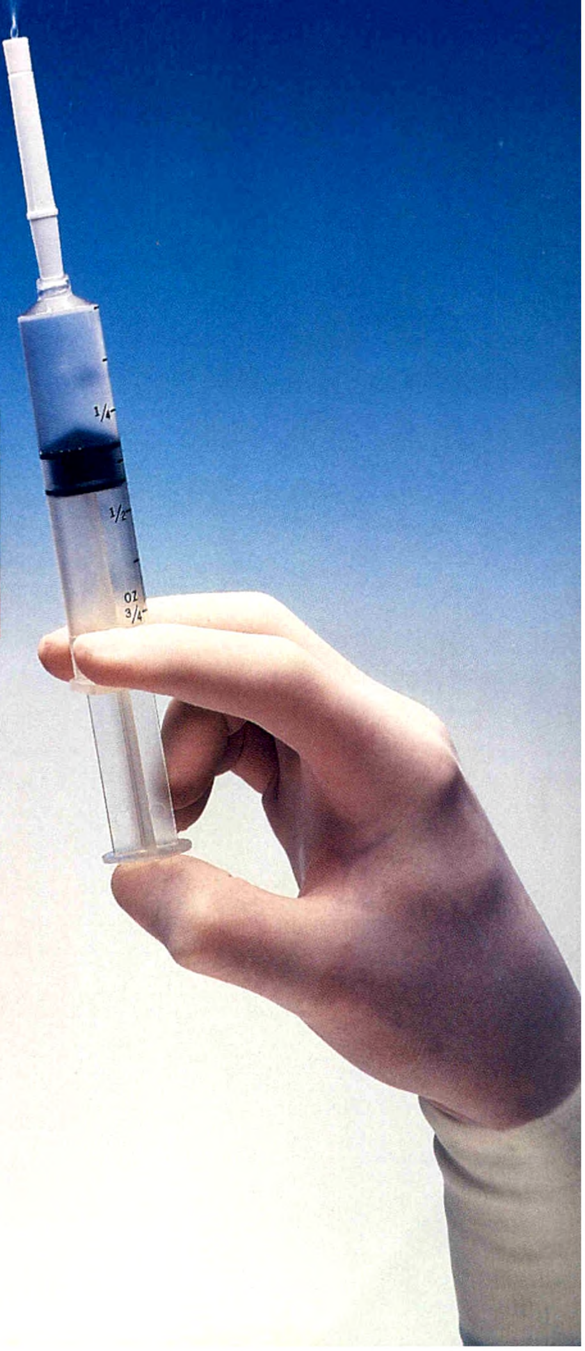

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DOSAGE AND ADMINISTRATION: General: Solutions of THROMBOGEN Thrombin may be prepared in sterile distilled water or isotonic saline. The intended use determines the strength of the solution to prepare. For general use in plastic surgery, dental extractions, skin grafting, neurosurgery, etc., solutions containing approximately 100 units per ml. are frequently used. For this, 10 ml. of diluent added to the 1,000 unit package is suitable. Where bleeding is profuse, as from cut surfaces of liver and spleen, concentrations as high as 1,000 to 2,000 units per ml. may be required. Intermediate strengths to suit the needs of the case may be prepared by selecting the proper strength package and dissolving the contents in an appropriate volume of diluent. In many situations, it may be advantageous to use THROMBOGEN Thrombin in dry form on oozing surfaces.

CAUTION: Solutions should be used immediately upon reconstitution. However, the solution may be refrigerated at 2–8°C, for up to three hours. The following techniques are suggested for the topical application of THROMBOGEN Thrombin.

1. The recipient surface should be sponged (not wiped) free of blood before THROMBOGEN Thrombin is applied.
2. A spray may be used or the surface may be flooded using a sterile syringe and small gauge needle. The most effective hemostasis results when the THROMBOGEN Thrombin mixes freely with the blood as soon as it reaches the surface.
3. In instances where THROMBOGEN Thrombin in dry form is needed, the vial is opened by removing the metal ring by flipping up the plastic cap and tearing counterclockwise. The rubber-diaphragm cap may be easily removed and the dried THROMBOGEN Thrombin is then broken up into a powder by means of a sterile glass rod or other suitable sterile instrument.
4. Sponging of treated surfaces should be avoided in order that the clot remain securely in place.
   THROMBOGEN Thrombin may be used in conjunction with Absorbable Gelatin Sponge, USP as follows:
   1. Prepare THROMBOGEN Thrombin solution of the desired strength.
   2. Immerse sponge strips of the desired size in the THROMBOGEN Thrombin solution. Knead the sponge strips vigorously with moistened gloved fingers to remove trapped air, thereby facilitating saturation of the sponge.
   3. Apply saturated sponge to bleeding area. Hold in place for 10 to 15 seconds with a pledget of cotton or a small gauze sponge.

THROMBOGEN Spray Kit: The THROMBOGEN Spray Kit contains one sterile vial of THROMBOGEN Thrombin, one sterile vial of isotonic saline diluent, one sterile disposable syringe and one sterile syringe spray tip. The kit may be used as follows:

1. Remove the Tyvek† blister lid from the outermost tray by pulling up at the indicated corner. The sterile inner tray can then be lifted out or introduced into the sterile field.
2. Remove the Tyvek† blister lid from the inner tray to expose the sterile contents.
3. Using the sterile syringe equipped with the needle, draw the desired amount of saline diluent from the vial into the syringe.
4. Inject the saline diluent into the THROMBOGEN Thrombin vial from the syringe to reconstitute the THROMBOGEN Thrombin powder.
5. When the THROMBOGEN Thrombin is completely dissolved, draw the THROMBOGEN Thrombin solution into the syringe.
6. Remove and discard the needle; affix spray tip by pushing down and turning clockwise until the spray tip locks in place.
7. Depress the syringe plunger in a normal fashion to dispense the THROMBOGEN Thrombin solution through the tip in a fine spray.
8. Alternatively, to facilitate using the THROMBOGEN Thrombin with an Absorbable Gelatin Sponge, USP, the THROMBOGEN Thrombin solution may be dispensed directly from the syringe into a sterile container vs. attaching the spray tip. When THROMBOGEN Thrombin is needed in the dry form, the vial is opened and the dried THROMBOGEN Thrombin pellet should be broken up into a powder with a sterile glass rod or other suitable instrument.

Caution: Federal law prohibits dispensing without a prescription.

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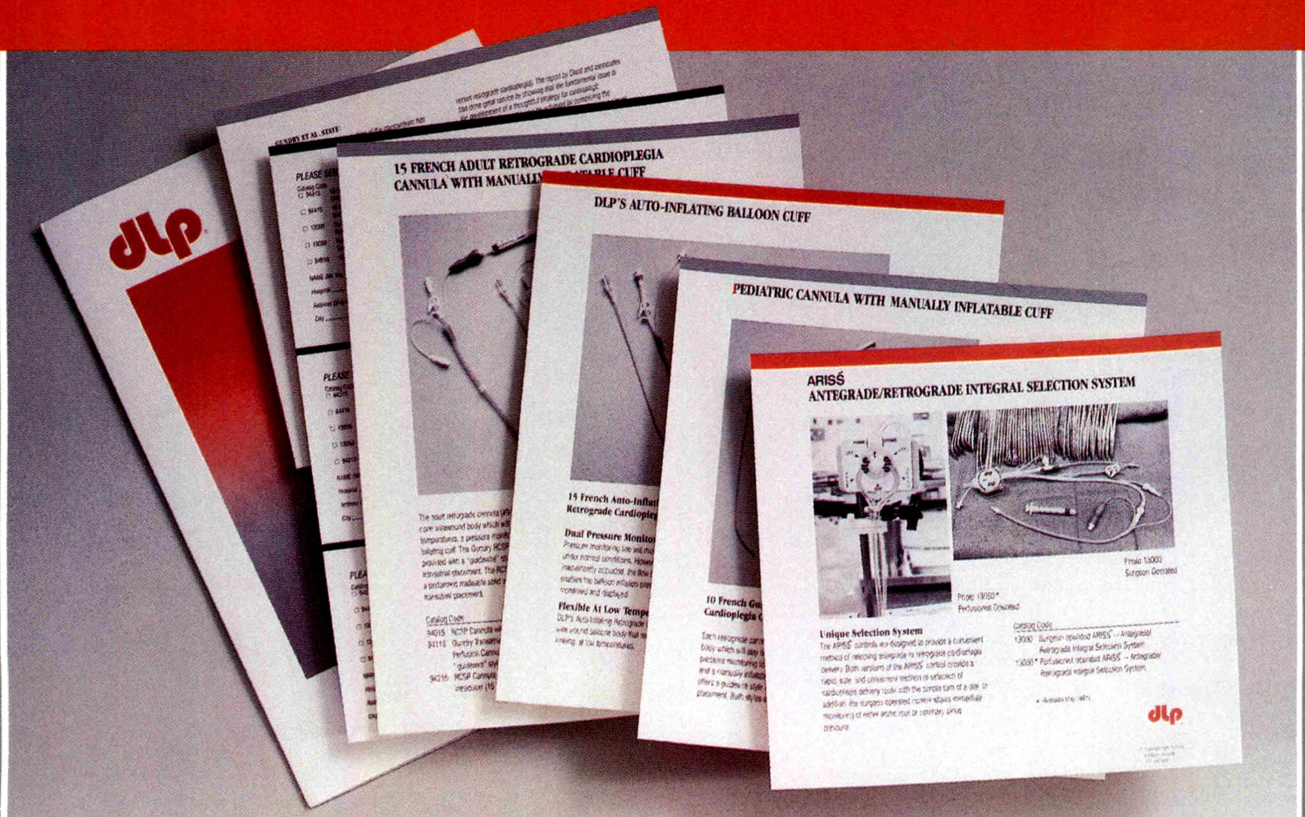
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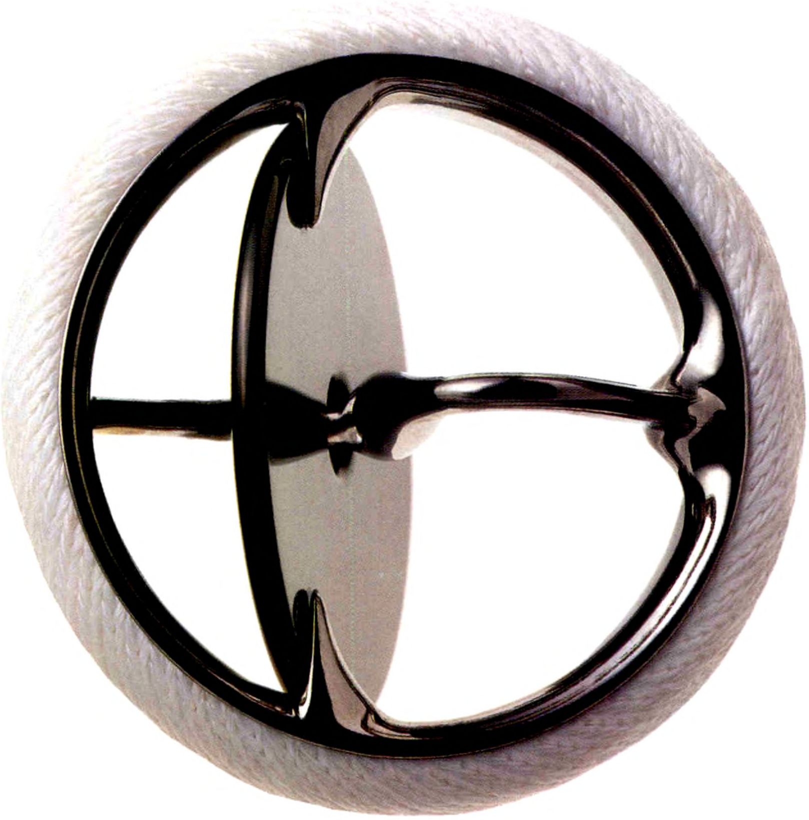

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REFERENCES

1. Data on file, Medtronic Heart Valves, Medtronic, Inc.
2. Grunkemeier GL, Rahimtoola SH. Artificial heart valves. *Annu Rev Med.* 1990;41:251-263.
3. Butchart EG, Lewis PA, Grunkemeier GL, et al. Low risk of thrombosis and serious embolic events despite low-intensity anticoagulation: Experience with 1,004 Medtronic Hall valves. *Circulation.* 1988;78 (suppl 1):166-177.
4. Tatineni S, Barner HB, Pearson AC, et al. Rest and exercise evaluation of St. Jude Medical and Medtronic Hall prostheses: Influence of primary lesion, valvular type, valvular size, and left ventricle function. *Circulation.* 1989;80 (suppl 1):116-123.
5. Nitter-Hauge S, Abdelnoor M. Ten-year experience with the Medtronic Hall valvular prostheses: A study of 1,104 patients. *Circulation,* 1989:80 (suppl 1):143-148.
6. Vallejo JL, Gonzalez-Santos JM, Albertos J, et al. Eight years' experience with the Medtronic Hall valve prosthesis. *Ann Surg.* 1990;50(3):429-436.
7. Grunkemeier GL. Medtronic Hall Prosthetic Heart Valve: A Review of Clinical Performance.

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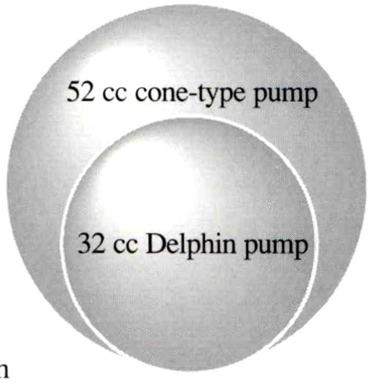
Air handling and centrifugal blood pumps

By far the most popular reason given for using centrifugal pumps is safety.[1] Certainly, the inability to pump gross air (a large bolus of air) is a significant safety advantage of centrifugal pumps. Yet not all centrifugal pumps perform equally well when it comes to air handling.

Protection against gross air

A large bolus of air will deprime a centrifugal pumphead. Once the pump is deprimed, the flow rate drops to 0 and the air is held up in the pumphead, though the pump continues to spin. Roller pumps, on the other hand, will continue to force air on towards the patient.

Just 32 cc of air will deprime a Delphin pumphead. Approximately 52 cc are required to deprime a cone-type centrifugal pump.[2] The Delphin pumphead protects patients by depriming with a relatively small amount of air.

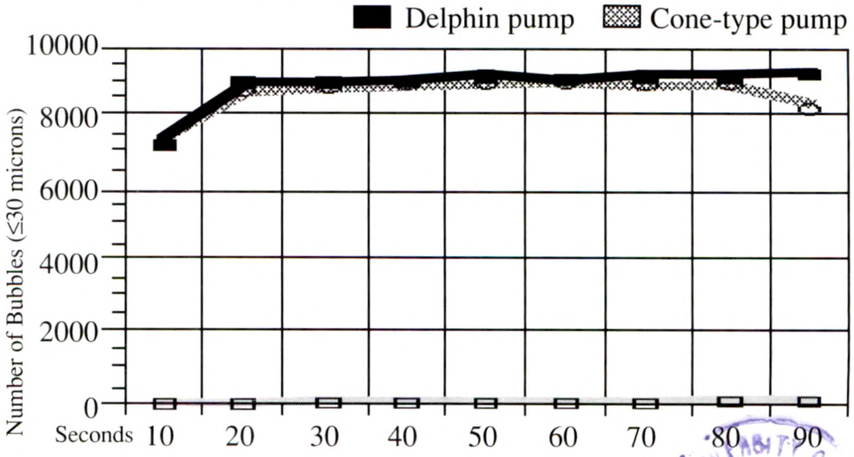


Air to deprime

Micro-air handling

All arterial pumps, including centrifugal pumps, will pump micro-air to some extent.[3] Under similar operating conditions, centrifugal pumps are essentially equivalent in their micro-air handling abilities.[4]

Micro-air handling



Although micro-air handling is essentially equivalent for all centrifugal pumps (as shown on this graph), the Delphin system deprimes with only 32 cc of air.

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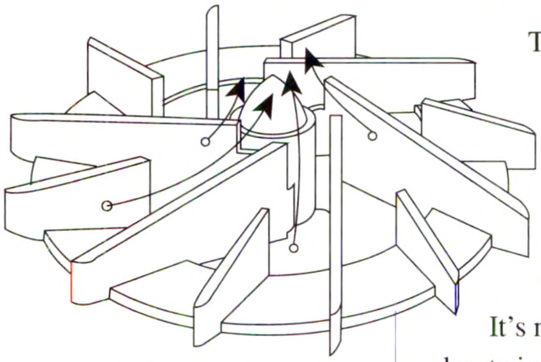
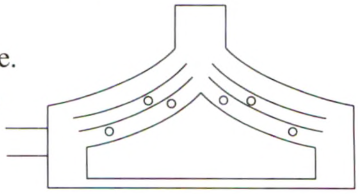
Easy debubbling



The open impeller design of the Delphin pumphead facilitates debubbling.

The open impeller design of the Delphin pumphead lends itself to convenient debubbling. Bubbles trapped beneath the cones are difficult to remove during priming. In an effort to debubble, many perfusionists resort to vigorously tapping the cone-type pumphead, a practice one manufacturer warns "may cause device malfunction."

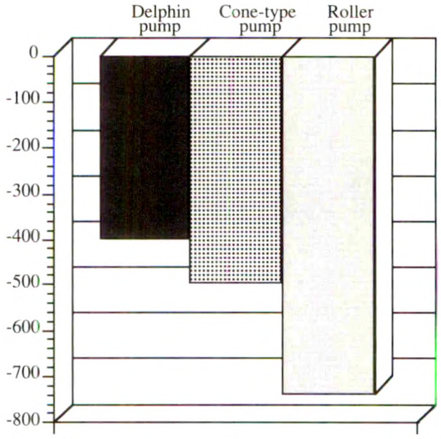
Tap the Delphin pumphead if you like. It's made of durable polycarbonate which has twice the impact strength of the acrylic used in some pumpheads[5].



The constrained design of cone-type pumpheads tends to trap bubbles during priming.

What about cavitation?

Cavitation, the sudden formation of micro-bubbles in solution, is caused by negative pressure. The greater the negative pressure potential at the pump inlet, the greater the risk of cavitation. Conversely, the lower the negative pressure, the greater the protection against cavitation. The Delphin system provides protection against cavitation by generating low levels of negative pressure. Should the inlet be occluded, the Delphin system produces less negative pressure than other pumping systems (for equivalent flow rates and pressure readings).



Negative pressure generated
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The Delphin pump protects against cavitation by generating low levels of negative pressure.

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Footnotes

[1] Based on a poll of *Heart-To-Heart* readers conducted in June, 1990. Almost three out of four respondents were already using a centrifugal pump for arterial perfusion (67%) or planned to (7%). A solid 26% did not use centrifugal pumps at all, and 15% were infrequent users.

[2] Pumps were flowing at 3.5 L/min with a pump outlet pressure of 300 mm Hg, a static pressure head of 30 mm Hg, and a mean arterial pressure of 60 mm Hg. To obtain these flow rates and pressures, the Delphin pump was operating at 2,350 RPMs, and the cone-type pump at 2,800 RPMs.

[3] Reed, Charles C. and Stafford, Trudi B. *Cardiopulmonary Bypass.* Houston: Texas Medical Press, Inc., 1985, p. 377.

[4] Numbers of 30 micron micro-bubbles were counted using a TLL Micro-bubble Activity Monitor attached near the centrifugal pump outlets following the introduction of 10 cc of air into each pumphead.

[5] Based on Izod impact of plastics testing for polycarbonate and acrylic using ASTM test method D256.

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(Continued)

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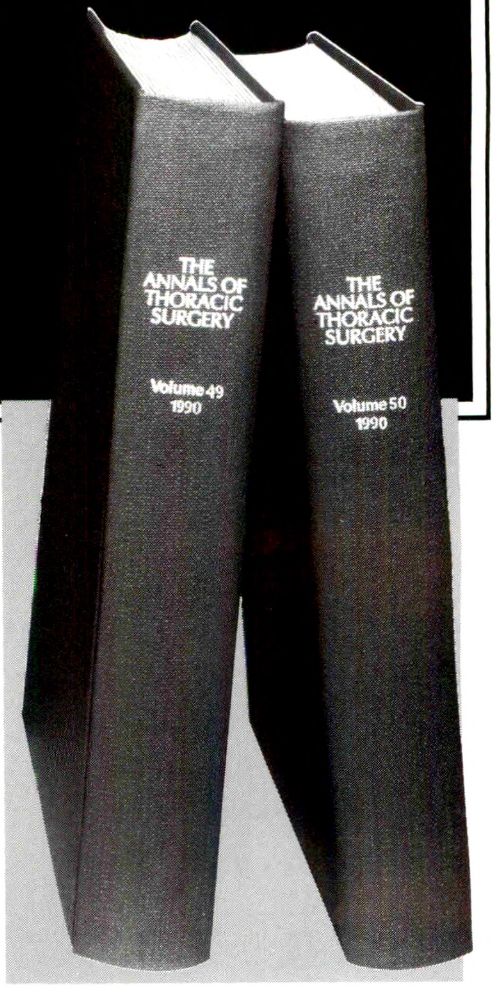
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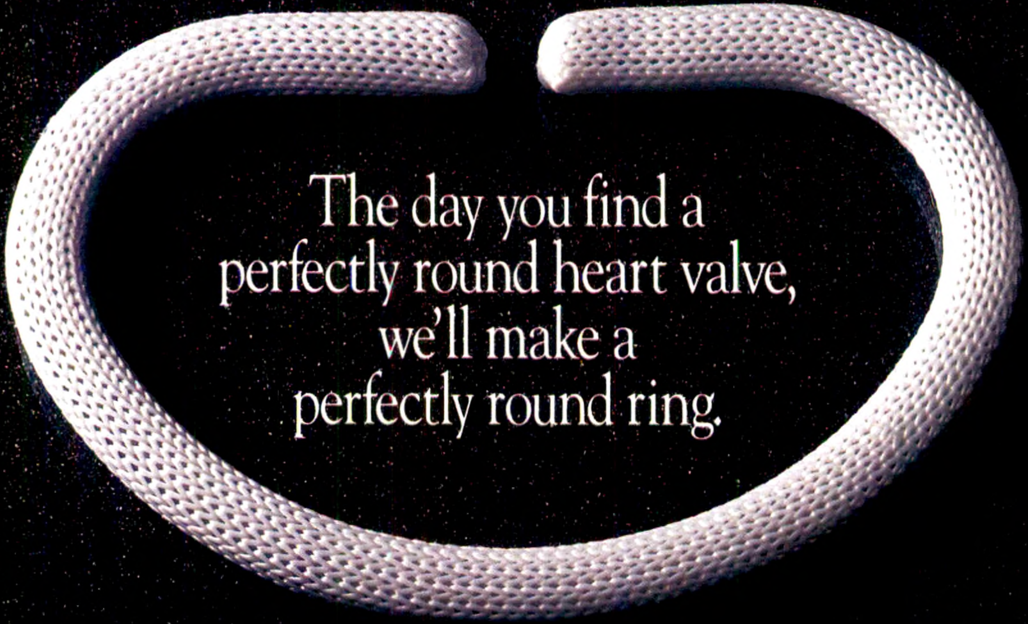

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Profiles of Leadership in Thoracic Surgery

W. Gerald Rainer, MD

Section of Cardiac Surgery, St. Joseph Hospital, and Department of Surgery, University of Colorado Health Sciences Center, Denver, Colorado

It was the best of times,
It was the worst of times,
It was the age of wisdom,
It was the age of foolishness,
It was the epoch of belief,
It was the epoch of incredulity,
It was the season of Light,
It was the season of Darkness,
It was the spring of hope,
It was the winter of despair.
Dickens [1]

Charles Dickens might easily have been one of The Society's representatives to a conference with one of the governmental agencies discussing resource-based relative value scales, physician reimbursement, and new CPT codes for redo coronary artery bypass or pulmonary lobectomy.

Since becoming a founding member of The Society of Thoracic Surgeons and having served with Drs Robert K. Brown and Alan Hopeman as the local arrangements committee for the second annual meeting of The Society in 1966, I have been impressed with the character of our leaders, having had an opportunity to work with almost all of them while serving on various committees and as secretary of The Society. I have tried to observe traits and characteristics of these thoracic surgeons that made them leaders of one of our specialty's major organizations. I became acutely aware that these people had qualities that were distinctive and set them apart from the average thoracic and cardiovascular surgeon. In enumerating some of these qualities, I do not for one moment mean to overlook some of our other great leaders or even to pass over some of the traits of leadership of some of those that I have chosen to exemplify today. I merely intend to recount some of the observations that I have made over the years that were impressive to me and have had a significant influence in my professional society development.

I have divided these segments, arbitrarily, into three periods: 1941–1981—the early years of our Society; 1981–1991—a more current era; and 1991 to the future, to enscribe what I perceive to be some of the requirements of our future leaders. These qualities are in no particular order of importance, nor is the list meant to be totally comprehensive.

The first characteristic of leadership is that of **Loyalty**. I can think of no two individuals who exemplify this feature more than Drs Robert G. Ellison and Herbert Sloan. Doctor Ellison captures the essence of this in his magnificent dissertation during his presidential address entitled "Significant events in the history of The Society of Thoracic Surgeons" [2]. In this, Dr Ellison describes the beginning days of The Society, the drafting of its early constitution, and the efforts that the founders expended to make certain that The Society would be accepted in its then-current environment. I would recommend it for reading by all incoming members to obtain a better understanding of the very foundation of our organization. Doctor Ellison has continued in his demonstration of loyalty to our group by serving unstintingly since its inception, being our current historian and chairman of our Committee on By-Laws.

Doctor Herbert Sloan has served not only as president of The Society but also as the editor of *The Annals of Thoracic Surgery* for many years. I was profoundly impressed by his presidential address to the American Association for Thoracic Surgery entitled "Let us now praise famous men." This is truly a tribute to all of the members of our Society including those who support our cause and ideals by their everyday work, their dispensation of responsibility in their hospitals and communities, and their imparting of qualities that we should like to preserve in our specialty for those who come after us. These members, even though they may never appear in visible leadership positions, have vitally important roles

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Presented at the Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons, San Francisco, CA, Feb 18–20, 1991.

Address reprint requests to Dr Rainer, 2005 Franklin St, Suite 700, Denver, CO 80205.

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in the preservation and the continuation of our Society. Doctor Sloan [3] paraphrases Rudyard Kipling when he states:

> Let us now praise famous men
> Men of little showing
> For their work continueth
> And their work continueth
> Greater than their knowing.

This was adapted by Rudyard Kipling after a verse in Ecclesiasticus from the Apochrypha and is certainly a praise to the loyalty of all of our leaders and members.

Lest one be deceived, let me iterate that all of these leaders who I shall describe today have a multitude of enviable qualities and I have merely abstracted isolated characteristics to illustrate some of these points for this address.

The next profile that I have chosen is that of **Determination**. Perhaps no one could exemplify this trait more than J. Maxwell Chamberlain who, most would agree, had as much if not more to do with the founding of our Society than any other person. His accomplishments and exploits are legendary, and his determination to succeed is largely responsible for the position of our Society in our environment today. I have extracted a single sentence from the letter that Dr Chamberlain sent to thoracic surgeons across the country in September 1963 asking them to consider joining the newly formed organization [4].

> The union, therefore, of those engaged solely in the highest type of thoracic surgical performance dignifies and justifies the creation of a society for thoracic surgeons—a society designed to complement other related societies.

Certainly Dr Chamberlain was acutely aware of the perspective with which a group of young thoracic surgeons might be seen in trying to organize an association where all qualified thoracic surgeons could belong and have the feeling of the right of membership. His concept of this position in The Society's future has been validated many times over. I would hope that if Dr Chamberlain could look upon The Society today he would be pleased with the way it has interacted with other organizations and has responded to situations that arise in our current ever-changing practice environment.

Although all of the leaders of this Society and a large portion of the membership-at-large have exemplified **Excellence in Clinical Practice and Education**, there are two of our previous presidents who seem to exemplify these traits most appropriately. Thomas Ferguson, who earlier received The Society's Sixth Distinguished Service Award, has certainly become a role model for many thoracic and cardiovascular surgeons with a continuing series of accomplishments, honors, and recognitions. To become president of both major thoracic surgical organizations and to be involved heavily with the American Board of Thoracic Surgery and many related organizations such as the American Board of Medical Specialities and the Council of Medical Specialty Societies, and at the same time to carry out an active clinical practice and an active teaching schedule, are certainly enviable achievements. Add to that the current duties of editor of *The Annals of Thoracic Surgery* and one has a truly remarkable individual indeed. In spite of all these time-demanding activities, Dr Ferguson was able to set a tone that should serve as a model for all of us in his presidential address to the 13th annual meeting of The Society in 1977 [5] in which he stated:

> No matter how complex the distribution of health care becomes . . . the most satisfactory and successful care is . . . a one-to-one relationship between the patient and the physician.

This would tend to portray Dr Ferguson as one who, as many of us do after being heavily involved in Society and organizational affairs, enjoys a return to the bedside with physician-patient contact, which is one of the most rewarding feelings that we can experience and certainly the raison d'être of our specialty.

Doctor Hassan Najafi, the 18th president of our Society, has also excelled in the fields of education and practice. In addition to serving admirably as a director and then president of the American Board of Thoracic Surgery and having served this Society extremely effectively as the chairman of the Committee on Standards and Ethics prior to his becoming president, Dr Najafi used uncanny insight when he, in his presidential address [6], stated:

> With the exception of peace, no social ideal deserves more homage than education.

How more succinctly could one phrase the perceptive and insightful focus on two of our most noble aims? For such insight and perspicacity, we are forever grateful for having a member such as Dr Najafi serve as one of our leaders.

Compassion is a trait that should accompany us certainly from the time we enter medical school and should serve as one of the strongest forces directing our relationships with others. This involves not only the compassion that we should have for our patients but for all of humanity (Fig 1). We, as physicians and thoracic surgeons, cannot afford to look the other way when there are such compelling social issues facing us at every turn. The Society has played an active role in numerous seminars discussing the impact of the acquired immunodeficiency syndrome epidemic on its victims, health professionals, and society. We have not been as active as we might in the areas of social concern such as the homeless and the provision of quality medical care for all who are afflicted regardless of their ability to pay. One of our past presidents, F. Henry Ellis, Jr, was obviously acutely aware of these issues. He even chose a fitting title for his presidential address to the 14th annual meeting of our Society—"Caritas chirurgi" [7]. In his oration, he quotes Frances Peabody as follows:

> One of essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.

This was echoed and amplified by one of our honorary members for whom I have always had the greatest respect and admiration, Dr Dwight C. McGoon. Doctor McGoon

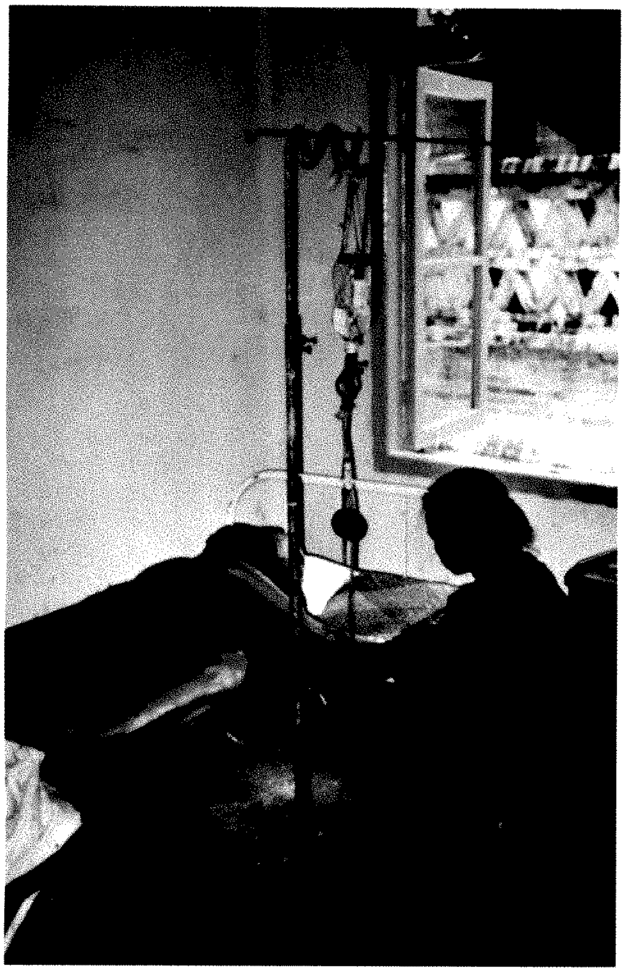

Fig 1. Compassion. Photograph of patient being comforted by her sister. (Taken by the author, Hsinhua Commune Hospital, Peoples Republic of China, 1978.)

has served as a paragon of virtue, all the while accomplishing great technical strides in the advancement of our specialty. In his Gibbon lecture to The American College of Surgeons in 1982 [8] he speaks of various factors that act upon the "dimensions of surgical progress." Here he states:

> To recognize that the ultimate purpose of our endeavor is the expression and manifestation of compassion for suffering humanity gives orientation to our professional motivation and gives hope and example to all of humanity.

Doctor McGoon, himself, certainly represents the embodiment of that motivation and hope.

During this early period that I have chosen to discuss, there has been an increasing need for nonsurgical skills in addition to the ones mentioned heretofore. Serving as leaders in thoracic surgery has required our spokepersons to be articulate and to demonstrate a character of **Statesmanship** heretofore unfamiliar to us because we have been compelled to deal with issues outside of the operating room, patient bedside, and our office of clinical activities. Our 14th president, Harold V. Liddle, obviously was aware of this and was one of our first leaders to perceive the winds of change of the sociopolitical environment into which we have been inexorably propelled. In his address to this assembly in 1979, Doctor Liddle states [9]:

> The doctrinaire proponents of egalitarianism avidly seek to change our present system of health care delivery, notwithstanding that egalitarianism is profligate, genetically impossible, and destructive of the American character of achievement.

That one concise statement summarized where we stood at that time "at the cross roads." Through such remarkable insight of some of our leaders such as Dr Liddle, The Society has structured its activities and its course in attempts to deal with these outside alien forces and at the same time has preserved our educational and scientific efforts. The Society has attempted to speak for our members who represent the vast majority of those involved in the everyday clinical practice of thoracic and cardiovascular surgery.

Knowing of their close relationship, I imagine that some of the articulate and statesmanship qualities that Dr Liddle demonstrated were learned, in no little measure, from his association with Ralph D. Alley, our 11th president. Certainly no one would deny that Dr Alley has been a magnificent statesman and spokesman for our interests in all areas of the sociopolitical and professional arenas. Although Dr Alley could have been used as an example of every single profile that I have mentioned up to this time, I simply have chosen statesmanship to portray him to this audience. In his address to the 12th annual meeting of The Society, Dr Alley stated [10]:

> . . . policies must be initiated and directed by the Council (of the Society) . . . if the Council fails in this responsibility, the Society will cruise at sea without a rudder . . .

In this presidential address, Dr Alley outlined the history and course of The Society of Thoracic Surgeons and the preparation of The Society (due largely to Dr Alley's efforts) in contracting with Smith Bucklin for their services as our managing office, a decision that, at that time, was very farsighted and helped to prepare our organization for the years ahead. Without this step, The Society would have had much difficulty in coping with the issues and problems that have befallen us.

Last is the one profile that should be essential to all of us. Certainly it is a necessary element in the makeup of leadership. I speak now of **Ethics** and its importance to our everyday life. This particular trait should be the guiding force in the relationship not only between us and our community and patients but also with our colleagues. It affects our personal conduct in every aspect of our daily lives. To some degree, ethics is involved in almost everything that we do. Our concept of ethics is in danger of sustaining severe erosion because of the competitive environment forced upon us by the changes in the socioeconomic modes of practice that we face today. Competition for market share between institutions and competition between individual surgeons and groups of surgeons (and physicians as well) to satisfy their own particular

Table 1. Profiles of Leadership in Thoracic Surgery (ca 1941–1981)

- Loyalty
- Determination
- Excellence in Clinical Practice and Education
- Compassion
- Statesmanship
- Ethics

Table 3. Profiles of Leadership in Thoracic Surgery (ca 1991 ⟶)

All of Tables 1 and 2, plus

- Judgment of Values Without Greed
- Dignity

demands has produced enormous strains upon the very foundation and structure of ethics. It affects us when we think of all of the societal issues that I have mentioned. It will certainly hold us in good stead in the eyes of the public more than any one attribute, save that of compassion. In his presidential address to this assembly in 1985, Dr George Magovern outlined some of the problems facing us at that time (and now) and traced the thin line of the evolution of ethics over the last one hundred or so years. The title of his address was very appropriate—"How shall we then practice?" [11]. He described many alternatives that were facing us then, including those of negotiating quality of practice and even ethics, itself, for a price. He summed up his feelings at that time most magnificently by stating:

> Gentlemen, the profession is not for sale.

These profile characteristics are summarized in Table 1.

Now, having taken the time to describe some of the attributes that I perceived in some of our leaders until recent years, I will address changes in societal forces that have caused us to devote an enormous amount of energy and talent to subjects that have been foreign to us. Current leaders require all of the preceding attributes plus a number of other talents and qualities that will allow us to face these changes in the market place and in our everyday negotiations even within our own institutional structures. In addition, leaders of today must have knowledge of electronic technology and keep appraised of the enormous advances that occur in this field. They need to be able to communicate extremely well with everyone with whom they come in contact whether it be colleagues, institutional administrative personnel, or governmental agencies. Adaptability is essential in the ever-changing scene of health care delivery. Some knowledge of the fine art of business administration would place one in good stead in addressing issues that seem to arise daily. Finally, some knowledge of the fine points of political science might be advantageous in trying to understand the inner workings of governmental bureaucracy. These qualities are tabulated in Table 2. This might appear like a heavy agenda but many of our members have already mastered some of those requirements and will be much better prepared for leadership positions in the near future.

Table 2. Profiles of Leadership in Thoracic Surgery (ca 1981–1991)

All of Table 1 plus

- Advanced Degree (or equivalent) in Electronic Technology
- Master of Communication
- Adaptability
- Advanced Degree in Business Administration
- Graduate Studies in Political Science

What about the qualities of leadership that we perceive will be needed for advancing into the 21st century? We are only a few years short of that transition and, in spite of budgetary constraints of research and cost of practice, enormous strides continue to be made in the way we practice our specialty. The challenges brought about by these advances will require even new and, as yet undescribed, qualities that will have to be palpably perceived as time progresses. Hopefully, all of the profile characteristics that I have mentioned will not be forgotten. Hopefully, future leaders will be far better qualified than any of us up to the present for continuing to direct The Society in its proper course. Hopefully, the lessons of the past will not be forgotten because of problems of the future. I sincerely hope that our future leaders will try in every way possible not to forget that they must have all of the characteristics that we have mentioned for the first and second stages of today's presentation and, in addition, try to preserve two additional attributes (Table 3), **Judgment of Values Without Greed** and **Preservation of Dignity of our Profession and Specialty.**

In assessing the values of our services, great care must be taken to attempt to accurately and correctly establish the appropriate and precisely cross-linked values that should be attached to our services; this should be done not only for the purposes of monetary reimbursement but for the placement of the importance of our talents in the overall scheme of things.

In addition, dignity must be respected in all of our negotiations and interrelationships with all other specialties, societies, and agencies. Venturing into the "world outside of medicine" throws us into association with individuals and groups of individuals that may not have the same dignified approach to the solution of our mutual problems that we might have. The exhibition of dignity and patience in these negotiations will afford us the respect that should be due us and will help immeasurably in achieving our ultimate aims.

In addition to the qualities that I have outlined, it might be wise to ponder some areas that should be avoided.

Mahatma Gandhi summarized these very appropriately when he listed what he termed the "seven deadly sins" [12].

Wealth without work
Pleasure without conscience
Knowledge without character
Commerce without morality
Science without humanity
Worship without sacrifice
Politics without principle

In closing, I thank you for your patience in allowing me to provide a brief overview of some of the qualities of leadership that have been meaningful to me. I have shared with you some of my innermost observations and hope that they have helped direct me in trying to fulfill a leadership role for your Society by properly and appropriately representing what I perceive to be the most desirable elements and qualities of our specialty. For those of you who have concern about where our future leaders who possess all of the attributes that I have enumerated might come from, I would suggest that you look around you. Where are the giants of yesteryear? Where are the leaders of the future? Look around you; they are here.

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References

1. Dickens C. A tale of two cities. London: Chapman and Hall, 1859:1.
2. Ellison RG. Significant events in the history of The Society of Thoracic Surgeons. Ann Thorac Surg 1972;14:577–603.
3. Sloan H. Let us now praise famous men. J Thorac Cardiovasc Surg 1980;80:159–70.
4. Chamberlain JM. In: Ellison RG [2].
5. Ferguson TB. Guilds, boards and hobgoblins. Ann Thorac Surg 1977;24:6–18.
6. Najafi H. A fascinating journey. Ann Thorac Surg 1983;36: 1–9.
7. Ellis FH. Caritas chirurgi. Ann Thorac Surg 1978;26:6–10.
8. McGoon DC. The dimensions of surgical progress. Bull Am Coll Surg 1982;67:15–8.
9. Liddle HV. Impasse at the crossroads: evolution or regulation. Ann Thorac Surg 1979;28:7–13.
10. Alley RD. The Society of Thoracic Surgeons. Ann Thorac Surg 1976;22:407–14.
11. Magovern GJ. How shall we then practice? Ann Thorac Surg 1985;40:103–12.
12. Platt S, ed. Respectfully quoted: a dictionary of quotations from the Congressional Research Service. Washington, DC: Library of Congress, 1989:319.

Palliation of Univentricular Heart Without Increasing Ventricular Work

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Among the factors considered important in determining short-term and long-term survival as well as the quality of survival after the modified Fontan procedure are the pulmonary vascular resistance, the anatomy of the pulmonary arteries, the presence of systemic ventricular hypertrophy, the previous use of systemic to pulmonary artery shunts, the function of the atrioventricular valve, and the age of the patient. The current algorithm for the surgical treatment of infants born with a univentricular heart avoids volume and pressure overload of the single ventricle. Assuming the risk of a completed modified Fontan connection is increased during the first year of life, what alternatives are available? In this issue, Douville and associates [1] report their experience with the hemi-Fontan operation. Their approach allowed satisfactory palliation without exposing patients to the higher risk of a completed Fontan procedure or the potential long-term complications associated with a systemic to pulmonary artery shunt. The report provides detailed drawings of the operation. The reader can easily appreciate the technical details and the theoretical advantages of this approach to palliation.

The hemi-Fontan operation is one of several similar therapies available for patients considered at increased risk for the Fontan procedure. The bidirectional cavopulmonary shunt [2], the fenestrated Fontan [3], and the adjustable Fontan [4] are alternative operations. The bidirectional cavopulmonary shunt and the hemi-Fontan provide palliation by diverting only the superior vena caval blood flow directly to the lungs. The adjustable Fontan and the fenestrated Fontan divert a larger percentage of the systemic venous return and provide a means to nearly complete the Fontan procedure [5]. The adjustable Fontan and fenestrated Fontan may not require an additional open heart procedure for complete separation of the circulations.

See also page 893.

The hemi-Fontan should be compared and contrasted with the bidirectional cavopulmonary shunt. The hemi-Fontan procedure requires the use of cardiopulmonary bypass. During construction of the hemi-Fontan connection, pulmonary artery stenoses can be repaired and preexisting sources of pulmonary blood flow are eliminated. At the completion of the operation, volume overload of the ventricle is eliminated and the superior vena cava–right atrial junction is in continuity. In theory, completion of the Fontan procedure is straightforward, although another incision in the atrium is required along with excision of the superior vena cava baffle. The hemi-Fontan operation may facilitate the completion of the Fontan by the lateral tunnel or total cavopulmonary connection approach [6].

In contrast, the bidirectional cavopulmonary shunt can be performed without the use of cardiopulmonary bypass. Complications intrinsic to the use of cardiopulmonary bypass are avoided, the exposure to blood products is limited, and there is no intraatrial operation. The bidirectional cavopulmonary shunt can be added to existing pulmonary blood flow when the patient has inadequate pulmonary blood flow [2]. Although the ventricle is not totally unloaded, excellent palliation can be achieved. When a right thoracotomy is used, the pericardial opening is small and adhesions are minimized. In our series, 14 of 37 patients (38%) underwent the bidirectional cavopulmonary shunt without the use of cardiopulmonary bypass (no mortality).

Potential disadvantages of the bidirectional cavopulmonary shunt include division of the superior vena cava and, in some patients, the residual small volume load on the ventricle. Proponents of the hemi-Fontan procedure argue that the subsequent Fontan operation will be "easier" to perform. In our experience (11 patients), completion of the Fontan procedure has been straightforward when the intermediate palliative procedure was a bidirectional cavopulmonary shunt. We have been able to avoid the region of the sinoatrial node without difficulty. A flap of atrial wall may be turned superiorly and connected to the inferior surface of the right pulmonary artery, if necessary. This living anastomosis is roofed with a patch of pericardium, polytetrafluoroethylene, or homograft. In contrast, completion of the Fontan after the hemi-Fontan procedure requires a new atriotomy and excision of the superior vena cava patch. Insertion of the atrial septal patch or lateral tunnel baffle places additional suture lines within the scarred atrium and creates a potentially arrhythmogenic milieu.

Douville and associates [1] beautifully describe the hemi-Fontan procedure, and they define its role in the staged approach to the treatment of infants born with a univentricular heart. The bidirectional cavopulmonary shunt is an alternative to the hemi-Fontan procedure in the subset of patients who do not require reconstruction of the pulmonary arteries, control of excessive pulmonary blood flow, or repair of additional intracardiac lesions. The treatment of a patient born with a univentricular

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heart requires individualized therapy. There will be no single operation suitable for all patients. For example, a patient born with left-sided juxtaposition of the atrial appendages and a single right superior vena cava is ideally suited to the hemi-Fontan procedure. The lack of atrial tissue on the right side would hamper completion of the Fontan procedure if the cavoatrial junction were divided to perform a bidirectional cavopulmonary shunt. In summary, only long-term analysis including exercise testing and arrhythmia monitoring will allow definition of the "ideal" intermediate operation for an infant born with a univentricular heart.

References

1. Douville EC, Sade RM, Fyfe DA. Hemi-Fontan operation in surgery for single ventricle: a preliminary report. Ann Thorac Surg 1991;51:893–900.
2. Lamberti JJ, Spicer RL, Waldman JD, et al. The bidirectional cavopulmonary shunt. J Thorac Cardiovasc Surg 1990;100:22–30.
3. Bridges ND, Lock JE, Castaneda AR. Baffle fenestration with subsequent transcatheter closure. Modification of the Fontan operation for patients at increased risk. Circulation 1990;82:1681–9.
4. Pearl JM, Laks H, Drinkwater DC, Stein DG, George B, Williams R. The partial Fontan: advantages of an adjustable interatrial communication. Presented at the 27th Annual Meeting of The Society of Thoracic Surgeons, San Francisco, CA, Feb 18–20, 1991.
5. Laks H. The partial Fontan procedure. A new concept and its clinical application. Circulation 1990;82:1866–67.
6. Jonas RA, Castaneda AR. Modified Fontan procedure: atrial baffle and systemic venous to pulmonary artery anastamotic techniques. J Cardiac Surg 1988;3:91–6.

Cervical Lymph Node Dissection for Thoracic Esophageal Cancer

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In this issue, Kato and colleagues [1] from The National Cancer Center Hospital and National Oji Hospital in Tokyo report their experience with cervical lymph node dissection in patients undergoing resection of intrathoracic esophageal carcinoma. They compare two groups of patients operated on during the same time interval by two different groups of surgeons. Both surgical teams performed transthoracic esophagectomy with mediastinal and abdominal lymphadenectomy (two-field dissection). In group A patients, in addition, a bilateral cervical lymph node dissection was performed (three-field dissection). Group A patients undergoing the three-field dissection had a 5-year actuarial survival rate of 49% compared with 34% in the group B patients undergoing the two-field lymphadenectomy. Remarkably, in group A, the 4-year actuarial survival rate for 20 patients who had positive lymph nodes in the cervical dissection was 48%. Kato and colleagues conclude that cervical lymph node dissection is effective as a curative addition to radical operation for thoracic esophageal carcinoma. These provocative and excellent results deserve careful analysis and consideration.

See also page 931.

This was not a strictly randomized trial between two groups. In fact, the groups are probably dissimilar, so this report cannot be accepted as a valid comparison that proves that the addition of cervical lymph node dissection improves survival. Careful analysis shows consistent differences between the two groups suggesting that those treated without the neck dissection (group B) were a less favorable population for curative treatment.

For example, group B patients were 4 years older on average. A greater proportion in group B had tumors of the upper and mid esophagus whereas group A patients more often had carcinoma of the lower esophagus ($p < 0.05$). Tumor size averaged 0.4 cm greater in the group B patients. Although not significant, 34 of 73 group B patients (47%) had T3 or T4 staged tumors compared with 31 of 77 (40%) in group A. Similarly, 56% of group B patients had disease staged III or IV compared with 47% in group A. Similar data concerning the final pathological staging of the tumor also slightly favored group A patients. Kato and colleagues argue that the proportion of group B patients having positive but unresected lymph nodes in the neck may have been similar to the proportion of group A patients with proven positive cervical lymph nodes. If this is the case, group B is likely to contain a substantially greater number of patients with positive lymph nodes than in group A. Altogether these differences might account for the difference in survival rather than the extent of the operation.

There is evidence to suggest that the surgical techniques and outcomes were different between the two groups. For example, the mortality in group B was 10 of 73 (14%) compared with 5 of 77 (7%) in group A. There were more complications in group B, which incidence approaches statistical significance even though a more extensive operation was performed in group A requiring 3 hours of additional operating time. The group A patients, on average, had twice as many (33 more) lymph nodes removed. Although it is possible that all of these nodes came from the neck, it seems likely that a proportion of the increased number of lymph nodes may have come from a more thorough dissection of the mediastinum and abdomen as well. For these reasons, having groups of patients randomized between surgical teams instead of by patient produces a situation in which the two groups of patients are probably dissimilar and cannot be compared.

Nevertheless, the extraordinary 48% long-term survival rate of patients having positive cervical lymph nodes resected along with intrathoracic esophageal carcinoma is an important observation in its own right which deserves consideration for its implications in cancer surgery. Conventional thinking and teaching in the Western world is that positive lymph nodes at a remote distance from the primary tumor are equivalent to M1 or metastatic disease. In applying en bloc esophagectomy in attempted cure of intrathoracic esophageal carcinoma, the radical dissection is limited to 10 cm on either side of the tumor as the region to be included within the curative field. Lymph nodes beyond this point are regarded as evidence of systemic or metastatic disease [2]. For this reason, cervical lymph node dissection is performed as part of curative operation for upper-third or cervical esophageal cancer but not for middle- or lower-third intrathoracic carcinoma. If the results reported by Kato and colleagues are validated in other experiences, and in other geographic regions, this concept of extended lymph node dissection may have to be revisited. Other reports from Japan offer some support for extending the lymph node dissection for esophageal cancer, but the advantages in survival are not yet clearly established [3, 4]. This concept runs counter to current popular recommendations about curative therapy for other cancers, in particular, breast carcinoma.

The extensive lymph node dissection as practiced in

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Japan varies in its philosophy and technique from the en bloc resection as practiced in North America and Europe [5, 6]. The objective of the en bloc resection is to remove a complete, intact envelope of tissues surrounding the primary tumor in the mediastinum. This incorporates not only lymph nodes, but the tissues adjacent to the esophagus in which microscopic spread from early wall penetration may occur. Excellent local control of the primary tumor in the mediastinum is obtained by this approach. Patients with early spread to one to four lymph nodes in the region or early wall penetration have long-term survival comparable with that described by Kato and colleagues. In our series [2], 3-year survival for patients having either, but not both, wall penetration or positive lymph nodes is 44% and 50% compared with the 50% three-year survival for stage III patients in group A in this paper. Whether results can be improved by extending the en bloc dissection to include cervical lymph nodes is unknown.

Before considering extension of the operation, attention must be directed to potential complications. The major difference between this Japanese experience and the results of en bloc resection appears to be the incidence of vocal cord paralysis. The 14% incidence of vocal cord paralysis with extended cervical lymph node dissection is considerably greater than the 2% incidence with en bloc resection of the mediastinum [7]. However, the patients with two-field dissection in the Japanese report also had a high risk of vocal cord paralysis, suggesting that the lymphadenectomy techniques themselves may account for this rather than the third field of dissection.

Analysis of the site of recurrence in patients with adenocarcinoma arising in Barrett's esophagus in the lower or mid esophagus demonstrated that 4 of 20 patients in our series who died of metastatic disease had recurrences in cervical lymph nodes [8]. In contrast, only 1 patient treated by the en bloc resection had the recurrence primarily in the mediastinum. These results suggest that attention should be paid to the question of removing cervical lymph nodes.

At this point, the controversy persists. Two interpretations may be placed on the report by Kato and colleagues. One would be to agree with the authors that removal of positive cervical lymph nodes may contribute to prolonged survival, although this is not proved by the comparison of the two groups in this paper. The other interpretation is that although cervical lymph nodes may be positive in patients with intrathoracic esophageal cancer, the removal of these lymph nodes may not be related to long-term patient survival. As other reports come forth from surgeons practicing the extended lymph node dissection, the answer will become clearer as to whether this should be considered part of a curative operation for esophageal cancer. A properly randomized, prospective trial may be necessary to settle this controversy.

References

1. Kato H, Watanabe H, Tachimori Y, Iizuka T. Evaluation of neck lymph node dissection for thoracic esophageal carcinoma. Ann Thorac Surg 1991;51:931–5.
2. Skinner DB, Ferguson MK, Soriano A, Little AG, Staszak VM. Selection of operation for esophageal cancer based on staging. Ann Surg 1986;204:391–401.
3. Tsurumaru M, Akiyama H, Udagawa H, Ono Y, Suzuki M, Watanabe G. Cervical-thoracic-abdominal lymph node dissection for intrathoracic esophageal carcinoma. In: Ferguson MK, Little AG, Skinner DB, eds. Diseases of the esophagus. Malignant diseases, vol 1. New York: Futura, 1990:21.
4. Ide H, Hanyu F, Murata Y, Kobayashi A, Yamada A, Kobayashi S. Extended dissection for thoracic esophageal cancer based on preoperative staging. In: Ferguson MK, Little AG, Skinner DB, eds. Diseases of the esophagus. Malignant diseases, vol 1. New York: Futura, 1990:20.
5. Skinner DB. En bloc resection for neoplasms of the esophagus and cardia. J Thorac Cardiovasc Surg 1983;85:59–71.
6. Siewert JR, Holscher AH, Adolf J, Bartels H, Holscher M, Weiser HF. Esophageal cancer: subtotal esophagectomy with mediastinal lymphadenectomy and esophageal reconstruction with delayed urgency. In: Siewert JR, Holscher AH, eds. Diseases of the esophagus. New York: Springer-Verlag, 1987.
7. Skinner DB, Belsey RHR. Resection for potentially curable esophageal cancer. In: Management of esophageal disease. Philadelphia: W.B. Saunders, 1988:49.
8. Altorki NK, Skinner DB, Ferguson MK, Little AG. Barrett's adenocarcinoma: long-term survival and recurrence patterns. In: Ferguson MK, Little AG, Skinner DB, eds. Diseases of the esophagus. Malignant diseases, vol 1. New York: Futura, 1990:26.

Supravalvar Aortic Stenosis

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Supravalvar aortic stenosis is the least common form of left ventricular outflow obstruction. An individual experience, therefore, is seldom more than a few cases. In this issue, Sharma and associates [1] present the total experience with operative treatment of supravalvar aortic stenosis at the Texas Heart Institute. The experience spans a 29-year period and comprises 73 patients, surely the largest single-institution experience ever reported. Reason would dictate that important inferences could be drawn from this vast experience and that the treatment of this condition could be clearly defined. On the contrary, Sharma and associates correctly conclude that certain forms of supravalvar aortic stenosis continue to pose a serious challenge to surgical treatment. Perhaps this is because even this large experience placed in perspective only amounts to 2 or 3 cases per year, making it difficult to learn from concurrent experience. As the experience accumulates, individual cases are treated individually, often based on anecdotal information or recall of most recent experience. Thus, only a careful analysis of the total experience will provide insight to the treatment of the full spectrum of the anatomical defect of supravalvar stenosis.

See also page 1031.

What have we learned from the Texas Heart Institute experience relative to supravalvar aortic stenosis? Sharma and associates have used standard classification of two forms of the defect based on what is done from a surgical viewpoint: localized and diffuse types. The localized form encompasses the so-called hourglass and membranous forms and was treated by a localized operation (patch aortoplasty). There is no data supplied relative to relief of left ventricular outflow obstruction, and the reader is left with the implication that a simple operation produced good results in the localized form of this anomaly. The diffuse form is a condition that involves not only the sinus rim but also the ascending aorta, arch, and arch arterial branches. The diffuse form was treated by a variety of operations including patch aortoplasty, left ventricular apex to aorta conduits, aortic resection with graft replacement, and extensive endarterectomy of the ascending aorta and arch with patch aortoplasty. In the diffuse form, these various operations have produced a variety of results, mostly poor, when taken in the long-term perspective. Yet Sharma and associates take much encouragement from recent results in treatment even in the most complex forms of the diffuse type of the anomaly.

One must do a bit of reading between the lines to come to the real inferences in the treatment of supravalvar aortic stenosis. Sharma and associates have actually subclassified the patients into four groups, which correctly implies a spectrum of anatomical defects identified in the aortic root and associated cardiac structures. There were 24 of 73 patients (32%) having the isolated, localized form of supravalvar aortic stenosis who were treated simply by patch aortoplasty. The results were good, with only one death occurring in the group (4%); no hemodynamic data were supplied. We can infer that about one third of the patients in the series had a simple anomaly that could be treated with a simple operation. Then we come to group 2: these are patients with a localized form of supravalvar aortic stenosis and some other associated obstructive lesion of the left ventricular outflow tract. This group comprised 33 of the 73 patients (45%). These patients required patch aortoplasty plus something else such as aortic valvotomy, aortic valve replacement, or subvalvar resection. From this we learn that about half of the patients with supravalvar aortic stenosis that is classified as simply localized actually have a complex anomaly of the left ventricular outflow tract. Supravalvar aortic stenosis should be considered as an anomaly that affects the entire aortic root rather than simply one that affects the sinus rim. Operations to correct this defect must be directed not only at widening out the supravalvar aorta but also at correcting other lesions in the left ventricular outflow tract. Patient groups 3 and 4 are those with a diffuse form of the defect and those in whom the defect is complicated by associated cardiac defects or infection, respectively. Here, the results are the least good commensurate with the severity and complexity of the composite of the defects.

Inferences from the total follow-up of these patients also require some reading between the lines. There is a long period of follow-up extending to 29 years but little information is provided as regards actuarial occurrence of reoperation, death, and other complications. Hazard analysis has not been done. What we know is that 16 of the 73 required a second operation (22%) at some time during the follow-up period, and that 5 patients died late after operation for complex forms of the defect. These data suggest that operations for supravalvar aortic stenosis are palliative and many, if not all, patients will eventually require other operations during their life course.

Supravalvar aortic stenosis should be thought of as a complex anomaly of the aortic root. Too often the surgeon focuses attention on only the defect at the sinus rim. The narrowing and thickening of the sinus rim is fundamental to the morphology of the defect, but there is more to

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understanding this defect. There is thickening of the aortic media and intimal hyperplasia resulting in reduction of the aortic circumference at the sinus rim. The morphological process may not be circumferential but may only involve the sinus rim over one or two sinuses. The sinus of Valsalva beneath the thick and short sinus rim may be abnormal or hypoplastic. The ostia of the coronary arteries may be obstructed by the overhanging thick sinus rim as well as a bound-down aortic cusp. The aortic valve cusps are reported to be thickened in about 30% of patients with supravalvar aortic stenosis [2]. The aortic valves are actually involved in every case because the relationships of the commissures are distorted as they are drawn close together by the shortened and thickened sinus rim. This distortion produces a characteristic buckling of the free edge of the aortic valve as the normal length accommodates for the shortened space at the sinus rim. The buckled aortic cusps become part of the obstruction within a space too small to accommodate them properly. The free edge of the aortic cusps usually has normal length in most young patients. Thickening of the edges of the aortic cusps, however, eventually accompanies turbulent blood flow associated with stenosis at the sinus rim. The thickened valve cusps then become an even more important part of the stenosing process. Primary abnormality of the aortic cusps such as bicuspid valve or commissural fusion is often associated with supravalvar aortic stenosis. The edge of the aortic valve cusp may become adherent to the aortic wall, isolating the aortic sinus and completely closing the coronary ostia. Subvalvar stenosis of the left ventricular outflow tract may be part of this total deformity of the aortic root.

Operation to relieve left ventricular outflow tract obstruction caused by the localized form of supravalvar aortic stenosis may be accomplished in many cases simply by placing a diamond-shaped patch across the sinus rim in the noncoronary sinus of Valsalva. This is the classic operation and will usually reduce or eliminate pressure gradients between the left ventricle and the ascending aorta. Unfortunately, this operation will accomplish little in rebuilding or remodeling the rest of the aortic root abnormalities that usually accompany thickening and narrowing of the sinus rim. It would seem that operations that achieve the best reconstruction of the entire aortic root will have the best chance of giving the patient a better early result and a longer period of time until something more has to be done to the aortic valve or the aortic root. Several years ago my colleagues and I [3] proposed an extended patch aortoplasty in hopes of achieving a more symmetric reconstruction of the aortic root. The sinus rim was divided at two points opposite each other and the incisions extended into both the noncoronary sinus and the right coronary sinus between the right coronary ostium and the commissure between the left and right cusps of the aortic valve. It should be noted that Figure 3G and H in the report by Sharma and associates [1] illustrates a second incision placed anterior to the right coronary ostium, which locates the incisions at perhaps 120 degrees around the circumference from each other rather than exactly across the circumference at 180 degrees as we have proposed. The location of the incision as they have shown it is not as symmetric as what we have described, and an incision in this position could place the right coronary artery at risk of injury as it courses anteriorly and to the right to reach the atrioventricular groove. Dividing the sinus rim at two points allows the noncoronary cusp and the right coronary cusp of the aortic valve to stretch out to normal length. The buckling of the valve is relieved as the halves of the aorta are separated anteriorly and posteriorly. The left cusp must also be treated either by resection of the supravalvar thickened rim or by incision into the left sinus of Valsalva to allow anterior displacement of one of the commissures of the valve. This is usually accomplished at the medial commissure but may also be done at the posterior commissure.

Once the valve cusps are freed up from entrapment by the supravalvar rim, the aortic sinus may be reconstructed by patch angioplasty. Incisions may even be extended into the ventricular septum or into the anterior leaflet of the mitral valve to relieve accompanying subvalvar obstruction with reconstruction continued to the aortic patch angioplasty. This will provide a symmetric reconstruction of the entire aortic root that, hopefully, will provide the best immediate relief of left ventricular outflow tract obstruction and long preservation of aortic valve function. This is speculative, of course, because we have no long-term supportive data. Sharma and associates have not provided these data either. We also understand completely that these reconstructive operations are accomplished by insertion of nonflexible prosthetic materials in the aortic root, which may not properly support the aortic valve over time.

Operations to correct the diffuse form of supravalvar aortic stenosis are less well defined. No individual surgeon gains much experience with this anomaly. Sharma and associates have provided 5 patients, 2 of whom were treated by a new approach: extensive endarterectomy of the ascending aorta and arch with patch aortoplasty extended to the aortic arch. This approach seems to be a good one because it is directed at the diffuse pathology of the anomaly. Because it is known that the morphological defect involves the media and intima, it is logical to remove that portion of the aortic wall by endarterectomy. Patch aortoplasty that is short of widening the entire ascending aorta and aortic arch will not correct the aortic obstruction. Sharma and associates are to be commended for providing this innovative approach to treatment of the diffuse form of this complex anomaly.

References

1. Sharma BK, Fujiwara H, Hallman GL, Ott DA, Reul GJ, Cooley DA. Supravalvar aortic stenosis: a 29-year review of surgical experience. Ann Thorac Surg 1991;51:1031–9.
2. Williams JCP, Barratt-Boyes BG, Lowe JB. Supravalvar aortic stenosis. Circulation 1961;24:1311.
3. Doty DB, Polansky DB, Jenson CB. Supravalvar aortic stenosis. J. Thorac Cardiovasc Surg 1977;74:362–71.

J. Maxwell Chamberlain Memorial Paper

Role of Staging in Prognosis and Management of Thymoma

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Eighty-five patients operated on for thymoma from 1972 to 1989 were evaluated, 32 with myasthenia gravis and 53 without. Masaoka staging revealed stage I disease in 45 (53%), stage II in 23 (27%), stage III in 14 (16%), and stage IVa in 3 (4%). There was no operative mortality. Actuarial survival at 10 years was 63.7% for all patients: 78.3% for those in stage I, 74.7% for those in stage II, and 20.8% for those in stage III. There was no recurrence in patients in stage I. Mediastinal recurrence developed in 4 patients in stage II considered to have noninvasive disease by the surgeon. It is recommended that all patients be followed up for a minimum of 10 years and that all patients in stages II and III receive postoperative radiotherapy. The presence of myasthenia gravis is no longer considered as an adverse factor in survival.

(Ann Thorac Surg 1991;51:888–92)

A quarter century ago at the American Association for Thoracic Surgery meeting, Edmunds [1] presented a seminal paper describing experience with surgical treatment of 63 patients with thymoma at the Massachusetts General Hospital (MGH). In it he concluded that the principal factors related to survival were "the invasive nature of the tumor and the presence of myasthenia gravis." Deaths from myasthenia were largely perioperative and have since that report largely been eliminated. The last myasthenia-related death after thymectomy at the MGH was in 1963.

The matter of thymoma invasion is not so clear, however. Castleman, the pathologist co-author of that paper, claimed "that he had difficulty defining the malignant potential from the histologic section" of those resected thymomas. Marchevsky and Kaneko [2] state "most encapsulated, benign thymomas have identical histologic and cytologic features to invasive, malignant thymomas." Rosai and Levine [3] take the position that the "surgeon is usually in a better position to assess the invasive nature of a thymoma from the findings at thoracotomy than the pathologist who examines the specimen after removal."

Thymoma is defined as a neoplasm of thymic epithelial cells. It is an unusual tumor with an infrequent potential for lymphatic or hematogenous spread while retaining a not uncommon capacity for local mediastinal invasion and apparent droplet metastasis to pleural surfaces. Excluded by this definition are other thymic tumors including Hodgkin's disease of the thymus (once labeled *granulomatous thymoma*), neuroendocrine carcinoid tumors (formerly *round cell thymoma*), and germinoma (seminoma) of the thymus.

This study was undertaken to assess the role of staging in determining prognosis in patients with thymoma and the need for adjuvant therapy after thymomectomy. In particular, it was designed to test the idea that the surgeon is indeed best suited to define thymoma encapsulation or invasion.

Material and Methods

The 18-year period from 1972 to 1989 inclusive was chosen for this review. It represents both an era of standardized experience on the General Thoracic Surgical Service at the MGH and an era in which myasthenia gravis has been eliminated as an adverse factor affecting survival of patients with thymoma. There were 85 patients with thymoma in this time interval representing 52% of an overall 50-year MGH surgical experience with 164 cases. The patients have been followed up a minimum of 1 year or to 10 years. Only 1 patient has been lost to follow-up.

Demographics

There was no predilection for age or sex as illustrated in vigesimal cohorts in Table 1 arranged by sex and the presence or absence of myasthenia gravis. The youngest patient was 13 years old; the eldest, 81 years old—both were female. The peak incidence in nonmyasthenic patients was in the group aged 50 to 69 years (27). In patients with myasthenia it was evenly divided between the 30 to 49 years cohort (11) and the 50 to 69 years cohort (12). There were 39 male and 46 female patients. There were 35 patients (41%) with myasthenia gravis and 50 (59%) without. Three of the 35 with myasthenia had development of symptoms only *after* thymomectomy. In each

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Table 1. Demographics of 85 Thymoma Patients: 39 Male, 46 Female

Ages (y)	Patients With Myasthenia		Patients Without Myasthenia	
	M	F	M	F
10–29	2	1	2	3
30–49	8	3	8	2
50–69	8	4	6	21
70–89	1	5	4	7
Total	19	13	20	33

instance the surgeon reported total removal of detectable thymic tissue. It can only be a matter of speculation whether these 3 patients, 2 women aged 18 and 67 years and a man aged 66 years, may indeed have had subclinical myasthenia gravis before operation.

Initial Symptoms

The clinical symptoms of these 85 patients were varied. The 32 patients with myasthenia gravis diagnosed preoperatively had neurologic symptoms, 23 systemic and 9 purely ocular. Of the remaining 53, 19 were asymptomatic and 9 had symptoms unrelated to the thorax that led to chest radiographs. In the final 25 patients there were 10 with chest pain, 6 with cough, 3 with dyspnea, 3 with intercurrent respiratory infection, and 1 each with superior vena caval obstruction, pure red blood cell aplasia, and hypogammaglobulinemia. These latter 2 represented the only evidence of autoimmune phenomena.

Radiology

Thymoma is the most common tumor of the anterior mediastinum. The diagnosis was suggested in each of the 85 patients by posteroanterior and lateral chest radiographs. In addition 25 underwent planar and 47 computed tomography. It was not clear how many of the latter examinations were carried out with contrast material. Special vascular studies were performed in 12 patients: 7 aortograms, 2 digital subtraction angiograms, 2 angiocardiograms, and 1 limited venogram. These were directed at the not uncommon differential diagnosis of vascular abnormality, principally aortic aneurysm. Only 2 patients were studied by magnetic resonance imaging. Only one fluoroscopic examination was actually carried out, a reflection of the use of modern imaging techniques.

Biopsy

It usually is not considered a necessary practice at MGH to have histologic or cytologic confirmation of the diagnosis of thymoma before operation. Needle aspiration biopsy was carried out in 5 patients of the 85, 4 by the fine-needle aspiration technique and 1 by a Vim-Silverman needle for histologic study. This was the 1 patient with pure red cell aplasia, an 81-year-old woman in whom this biopsy was the definitive procedure because of her precarious medical condition. Four other patients underwent a modified Chamberlain anterior mediastinotomy for diagnosis where the likelihood of thymoma was in considerable doubt or where preoperative radiotherapy was planned because of the enormity of tumor size. Mediastinoscopy was not useful in this series.

Operation

Exploration was carried out in 84 patients, 79 by median sternotomy and 5 by lateral thoracotomy. In 81 patients (95%) total removal of the thymoma was grossly possible; in 2, subtotal tumor resection was carried out; and in 1, biopsy only was the procedure elected in the face of extensive invasive disease. Total removal of all thymic substance was carried out in 75 cases. This is difficult in a strictly lateral thoracotomy. Two patients had undergone prior thymic operation elsewhere: 1, an incomplete cervical thymectomy for myasthenia gravis; the other, a lateral thoracic partial thymectomy 10 years previously for a tumor read (and reviewed) as hyperplasia.

Extended thymomectomy for invasive thymoma included lung in 11 cases (wedge excision 9 and lobectomy 2), a single phrenic nerve in 5 patients, the innominate vein in 3 patients, and separate pleural implants in 2 patients. Pericardium was resected in the course of operation on 17 patients.

Results

Staging

Pathologic staging of thymomas was introduced in 1978 by Bergh and associates [4]. Staging was carried out in this series according to the modification of Masaoka and co-workers [5]: stage I: macroscopic encapsulation (complete) and no microscopic invasion of capsule; stage II: macroscopic invasion into mediastinal fat or pleura or microscopic invasion into capsule; stage III: macroscopic invasion into pericardium, great vessels, or lung; stage IVa: pleural or pericardial dissemination; and stage IVb: lymphatic or hematogenous metastasis.

The results of staging were as follows: stage I, 45 (53%); stage II, 23 (27%); stage III, 14 (16%); and stage IVa, 3 (4%). In the 2 patients in whom subtotal thymoma removal only was possible, the staging was classified III. In the 2 in whom biopsy only was carried out, 1 (the elderly woman undergoing needle biopsy diagnosis) was labeled as having stage II disease at subsequent postmortem examination 9 months later and the other (Chamberlain biopsy and subsequent futile exploration) stage IVa.

An effort was made retrospectively to compare surgical with pathologic staging, particularly in light of the earlier reference that the surgeon is often better able to assess invasiveness. The retrospective surgical staging was arbitrary, using both careful review of the written operative record and personal interview with the individual surgeon. In this comparison there was one area of major difference. Six of the thymomas recorded as stage I by the surgeon were upgraded to stage II by the pathologist with the finding of either microscopic invasion of an apparently intact capsule or microscopic foci of tumor in mediastinal fat outside the primary tumor.

Table 2. Late Mortality in Follow-up of 85 Patients With Thymoma

	Postoperative Interval		
Stage	1 y	5 y	10 y
I	0	3	2
II	1	0	3 (2)[a]
III	3 (3)	2 (2)	2
IVa	0	0	2 (2)

[a] Numbers in parentheses are deaths due to recurrent thymoma or its treatment.

An effort to classify the tumors by histologic types as described by Bernatz and associates [6] was rather limited: epithelial, 17 (20%); lymphocytic, 16 (19%); mixed, 27 (32%); but not recorded by the pathologist, 25 (29%).

Survival

There was no operative mortality, defined as death within 30 days or as the result of an operative complication beginning in that interval of time. Subsequent mortality was categorized as early (within 1 year), intermediate (within 5 years), and long-term (within 10 years). These statistics in Table 2 are broken down into those thymoma-related or due to other causes. Exactly half of the 18 deaths occurring within 10 years were the result of either recurrent thymoma or the therapy for recurrence.

Survival was calculated by actuarial analysis as clarified by Grunkemeier and Starr [7]. Survival at 5 and 10 years is presented for all stages in Table 3 and for stages I, II, and III graphically in Figure 1. The 10-year actuarial survival for all 85 patients is 63.7%; for stage I patients it is 78.3%, for stage II 74.7%, and for stage III 20.8%. It is clear that the measure of survival for thymomas, often a slowly growing tumor even when invasive, is not indicative at 5 years. Four of the nine thymoma deaths were late, occurring between 5 and 10 years after operation.

There were no deaths from thymoma at any time in the 45 patients in stage I. None received adjuvant irradiation or chemotherapy, although 6 of the 16 patients with myasthenia gravis were managed after operation with steroids. In stage II patients there were two deaths from thymoma in the interval between 5 and 10 years, one in a patient who underwent postoperative irradiation and subsequent excision of recurrent tumor. Not all of the remaining seven thymoma-related deaths in stages III and IVa patients were specifically due to tumor. Three were cardiorespiratory deaths during or after radiotherapy, 1 was a suicide because of unrelenting pain, 1 was the result of respiratory arrest in a myasthenic patient, and 1 was in a myasthenic patient in stage IVa whose death was steroid-related.

Table 3. Actuarial Survival at 5 and 10 Years After Operation

	Postoperative Survival	
Stage	5 y	10 y
All tumors (n = 85)	87%	64%
I (n = 45)	90%	78%
II (n = 23)	96%	75%
III (n = 14)	58%	21%
IVa (n = 3)	. . .	. . .

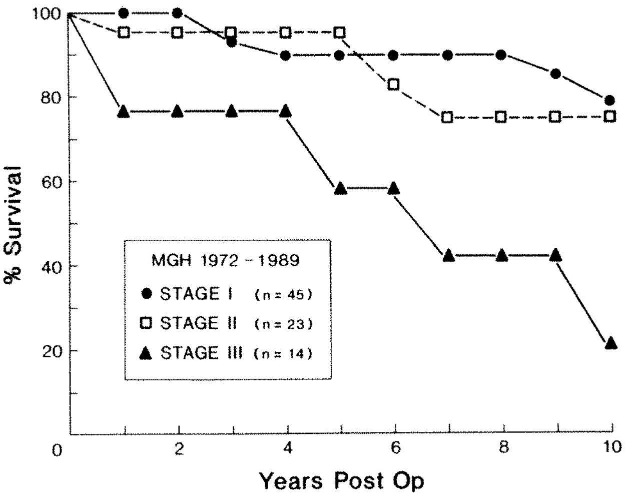

Fig 1. Actuarial survival versus pathological staging of thymoma (stages I and II versus III, p = 0.0001).

Most important was the development of recurrent thymoma in 4 stage II thymoma patients, each of whom was considered likely to be "cured" after the primary resection. Each subsequently underwent a secondary operation at which time all grossly detectable recurrence was successfully removed. Three of the 4 patients had myasthenia gravis. Although the survival curve for stage II patients duplicates that for stage I, freedom from thymoma recurrence is *not* duplicated.

Incidental mention is made of the survival of those thymoma patients with myasthenia gravis. Their 10-year actuarial survival is 71.6%, not statistically different from the 63.7% survival of the overall group. There is no difference in the incidence of thymoma stages between myasthenic and nonmyasthenic patients as demonstrated in Table 4. Two patients died of complications of myasthenia: 1 of a sudden respiratory arrest at 4½ years, the other of respiratory insufficiency at 6½ years.

Adjuvant Therapy

Adjuvant therapy was not carried out per protocol. Radiotherapy was delivered in 23 patients in doses varying between 30 and 60 Gy: in 8 of 23 stage II patients, 12 of 14

Table 4. Relationship of Myasthenia Gravis to Tumor Staging

	With Myasthenia Gravis		Without Myasthenia Gravis	
Stage	No.	%	No.	%
I	16	50	29	55
II	10	31	13	25
III	5	16	9	17
IVa	1	3	2	3

stage III patients, and all 3 stage IVa patients. Use of chemotherapy was limited to 1 stage IVa patient who died at 9½ years of a leukoencephalopathy.

Comment

What emerges clearly from this study is that patients with pathologic stage I thymoma, although they merit careful follow-up, need no adjuvant therapy and have an excellent prognosis. The same cannot be said for patients with stage II disease, 6 of whom were initially thought by the surgeon to be in stage I. The 10-year survival curves for patients with stage I and II thymoma are indeed superimposable. Nevertheless, whereas recurrent thymoma has not developed in any of the 45 stage I patients, it has developed in 5 patients with stage II disease (22%). As reported by Kirschner [8], resection of the recurrence was successful in 4 patients. It appears that the impression of the surgeon alone is not sufficient in assessing the likelihood of the development of further disease. Additional variables are needed in determining relative malignancy of thymoma.

Marino and Müller-Hermelink [9] have proposed a histologic classification of thymomas into cortical, medullary, and mixed subgroups. True medullary thymomas with rather small cells with irregular or spindle nuclei and no nucleoli are considered benign tumors. Cortical thymomas with larger epithelial cells, round or oval nuclei, and prominent nucleoli are malignant tumors. In the morphologic heterogeneity of thymomas many have a mixture of these elements. Using a combination of this histologic classification and the Masaoka staging, Pescarmona and associates [10] have proposed a rather complex prognostic grouping: stages I and II medullary types and stage I mixed type have an excellent prognosis, stages III and IV cortical types have a poor prognosis, and stages I and II cortical types plus stages II and III mixed types have an intermediate prognosis. Such a grouping will require ongoing studies for possible confirmation, but for the moment its very cumbersome indexing and the notoriously difficult pathologic challenge of classifying heterogeneous thymomas leave this approach to assessing malignancy and prognosis uncertain at best. Wick [11] finds the distinction "novel, though somewhat contentious."

The present study is interpreted to support another statement by Wick: "I believe that staging procedures predicated on the degree of tumor invasion are still the best prognosticators for thymoma." Invasion as determined by the surgeon, however, must be supplemented by histologic search by the pathologist for evidence of capsular invasion or the presence of microscopic foci within mediastinal fat. This is particularly true for stage II thymoma, which might otherwise be understaged and which, it has here been demonstrated, has a propensity for recurrence. Invasion in stage III thymomas is usually quite clear at gross assessment but here too evaluation by the pathologist to differentiate adherence from the true invasion of the lung, for example, is essential.

As a result of this analysis, it is suggested that (1) stage I patients require only careful follow-up, (2) stage II patients should undergo postoperative irradiation of the mediastinum and the entire operative field to a dosage of 50 Gy, and (3) stage III and IVa patients should undergo similar irradiation plus chemotherapy by a standard protocol to be determined by one's oncologic consultant. The principles of surgical approach remain basic, however. They include: (1) complete median sternotomy, (2) opening of both pleural sacs, (3) total thymectomy including all normal thymus, (4) extended resection in stage III situations, and (5) excision of all pleural implants in stage IVa.

The elimination of myasthenia gravis as a significant factor in long-term survival of patients with thymoma is in agreement with the Toronto group report in 1984 [12]. That paper also speculated on the use of preoperative radiotherapy in large, apparently invasive thymomas in an effort to reduce tumor bulk and to "prevent transpleural metastatic seeding at the time of operation." Although preoperative irradiation was employed in 2 patients in the series being reported, there is no evidence from this study to support or refute this appealing suggestion. The possibility of transpleural or local seeding of metastatic thymoma by preoperative biopsy (necessary to support preoperative irradiation) has led our group to advocate resection wherever possible without preliminary pathologic proof of diagnosis.

Maggi and colleagues [13] from the University of Torino have recently reported 241 cases with results that are generally supportive of the findings of this study. In addition, they find that the prognosis in patients with myasthenia gravis and thymoma is more favorable than in those without myasthenia, perhaps related to earlier detection of the tumor. They report that relapse of tumor in 108 patients with invasive thymoma was minimally affected by postoperative radiotherapy: 20.6% in patients receiving radiotherapy and 24.6% in those who did not. The effectiveness of radiotherapy, whether delivered preoperatively or postoperatively, merits further study. (The overall results of Maggi's 241 patients are indeed commendable: 86.9% of patients with encapsulated thymoma, 62% with local invasion, and 40% with pleural metastatic seeding are alive up to 10 years.)

From the present study, we draw the following conclusions.

1. Pathologic staging of thymomas by the method of Masaoka should supplement the gross surgical assessment of encapsulation of tumor versus invasion.
2. Stage I thymoma patients do not require adjuvant therapy but all stage II and III patients should receive postoperative radiotherapy.
3. Thymoma patients are at risk for late recurrence of their tumor and should be carefully followed up at least until 10 years. The 10-year actuarial survival should be the standard.
4. The presence of myasthenia gravis no longer has an adverse effect on survival in patients with thymoma.

References

1. Wilkins EW Jr, Edmunds LH, Castleman B. Cases of thymoma at the Massachusetts General Hospital. J Thorac Cardiovasc Surg 1966;52:322–30.
2. Marchevsky AM, Kaneko M. Surgical pathology of the mediastinum. New York: Raven Press, 1984:67.
3. Rosai J, Levine GD. Tumors of the thymus. Washington DC: Armed Forces Institute of Pathology, 1976:43.

4. Bergh NP, Gatzkinsky P, Larsson S, Lundin P, Rindell B. Tumors of the thymus and thymic region. I. Clinicopathological studies on thymoma. Ann Thorac Surg 1978;25:91–8.
5. Masoaka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymoma with special reference to their clinical stages. Cancer 1981;48:2485–92.
6. Bernatz PE, Harrison EG, Clagett OT. Thymoma: a clinicopathologic study. J Thorac Cardiovasc Surg 1961;42:424–44.
7. Grunkemeier Gl, Starr A. Actuarial analysis of surgical results: rationale and method. Ann Thorac Surg 1977;24:404–8.
8. Kirschner PA. Reoperation for thymoma: report of 23 cases. Ann Thorac Surg 1990;49:550–5.
9. Marino M, Müller-Hermelink HK. Thymoma and thymic carcinoma: relation of thymoma epithelial cells to the cortical and medullary differentiation of thymus. Virchows Arch [A] 1985;407:119–49.
10. Pescarmona E, Rendina EA, Venuta F, et al. Analysis of prognostic factors and clinicopathological staging of thymoma. Ann Thorac Surg 1990;50:534–8.
11. Wick MR. Assessing the prognosis of thymomas. Ann Thorac Surg 1990;50:521–2.
12. Shamji F, Pearson FG, Todd TRJ, Ginsberg RJ, Ilves R, Cooper JD. Results of surgical treatment for thymoma. J Thorac Cardiovasc Surg 1984;87:43–7.
13. Maggi G, Casadio C, Cavallo A, Cianci R, Molinatti M, Ruffini E. Thymoma: results of 241 operated cases. Ann Thorac Surg 1991;51:152–6.

DISCUSSION

DR PAUL A. KIRSCHNER (New York, NY): First, I want to congratulate Wilkins and associates on the selection of their paper to honor the memory of the late Dr J. Maxwell Chamberlain. I also appreciate the opportunity they granted me to review their manuscript in advance. They have presented a thorough analysis of the modern surgical management of thymoma, and their paper should stand as a model for future studies. Some points, however, may bear closer scrutiny.

Microscopy of thymoma is not dead. It plays a vital role in two aspects of staging despite the conventional teaching that surgical observations of invasion, not microscopy, determine the factor of malignancy.

The first is the incorporation in the Masaoka classification [1] of *microscopic* invasion of the capsule as well as the *gross* surgical observation as a determinant of stage II. Wilkins and associates note that six of their thymomas classified as stage I by the surgeons were upgraded to stage II by microscopy. Perhaps there should be a stage IIa and a stage IIb to resolve this problem.

The second aspect of microscopy deals with a new characterization of thymoma as a medullary, cortical, and mixed type based on the microscopy of the epithelial cell—the true thymoma tumor cell. This concept, proposed by Marino and Müller-Hermelink [2], has been shown by Pescarmona and associates [3] to correlate prognostically with the Masaoka staging system.

The medullary epithelial cells are elongated and spindle-shaped, and they display a whorled arrangement like fibroblasts. Cytoplasm is sparse and nucleoli are absent. On the other hand, the cortical thymoma is composed of larger cells with round or oval nuclei, prominent nucleoli, and abundant cytoplasm.

Medullary thymomas are completely encapsulated, do not recur after operation, and all turn out to be in stage I. On the other hand, mixed and purely cortical thymomas are found in the higher stages, tend to recur locally, and are associated with poorer survival. Postoperative radiotherapy and, in some cases, chemotherapy are recommended to improve long-term survival. It would be of interest to correlate Wilkins and associates' results in terms of this new classification. I note that 29% of their cases were unclassified and just called thymoma.

Still newer appraisal of thymoma is based on DNA nuclear content as determined by flow cytometry. Davies and co-workers [4] found that DNA aneuploid thymomas showed frequency of tumor recurrence and shorter relapse-free intervals than diploid tumors, independent of stage and histology. Asamura and associates [5] had less conclusive findings. More work is required on this area.

Wilkins and associates recommend radiotherapy in all stage II patients as well as in the higher stage patients. However, this is not risk-free treatment. Note that 3 patients in this report died of radiotherapy-related cardiorespiratory failure, not thymoma. Perhaps "fine-tuning" the staging of thymoma by adding the newer studies I have mentioned, ie, histology and DNA analysis, may direct the use of radiotherapy to wherever it will do the most good.

DR WILKINS: I thank Paul Kirschner for discussing this paper. For those of you with good memories, you will recall that I discussed his paper at the Baltimore meeting a year and a half ago, and this might look like a little home-and-home series, a little collusion. That perhaps is added to by the fact that he brought up some points in the paper that I did not have time to discuss this morning, and that is the matter of further pathologic investigation in terms of defining the malignancy of tumors. The work by Marino and Müller-Hermelink in Germany is the one that is receiving the greatest attention at this time. I cannot comment on how it affects the present series. I will say that Nancy Harris from our pathology department is now in the process of looking into this.

I emphasize, however, the other statement by Wick in his review in which he found that this newer pathologic classification was a bit complex and hard to use. He used the phrase "rather contentious." However, I do think there is room for further evaluation by some of the more sophisticated scientific methods, and perhaps if I am permitted to hear a paper in another decade, we will hear the answer.

References

1. Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymoma with special reference to their clinical stages. Cancer 1981;48:2485–92.
2. Marino M, Müller-Hermelink HK. Thymoma and thymic carcinoma: relation of thymoma epithelial cells to the cortical and medullary differentiation of thymus. Virchows Arch [A] 1985;407:119–49.
3. Pescarmona E, Rendina EA, Venuta F, et al. Analysis of prognostic factors and clinicopathological staging of thymoma. Ann Thorac Surg 1990;50:534–8.
4. Davies SE, Macartney JC, Camplejohn RS, et al. DNA flow cytometry of thymomas. Histopathology 1989;15:77–83.
5. Asamura H, Nakajima T, Mukai K, et al. Degree of malignancy of thymic epithelial tumors in terms of nuclear DNA content and nuclear area. Am J Pathol 1988;133:615–22.

Hemi-Fontan Operation in Surgery for Single Ventricle: A Preliminary Report

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Mortality after Fontan operation is related to risk factors like ventricular hypertrophy, pulmonary artery deformity, and young age (infancy). Preliminary procedures may improve Fontan results. The hemi-Fontan operation includes atriopulmonary anastomosis and correction of all anatomical risk factors, but an atriopulmonary patch directs superior vena caval flow into both pulmonary arteries and inferior vena caval flow into the ventricle, thus maintaining cardiac output (modified Glenn physiology). We performed 17 hemi-Fontan procedures in 16 patients, 14 primarily (median age, 9 months) and 3 for takedown of a Fontan operation. The 14 primary operations were for hypoplastic left heart syndrome (5), pulmonary atresia with intact ventricular septum (4), and other (5). All patients had multiple risk factors. Extubation was at 18 hours (median), chest tube removal was at 3 days, and hospital discharge was at 8 days postoperatively. Important complications included subglottic stenosis, transient diaphragmatic paralysis, pulmonary artery stenosis and thrombosis requiring reoperation, and transient ventricular fibrillation. One patient required hemi-Fontan takedown, and this patient later (3 months postoperatively) became the only death. Fontan takedowns have had a high mortality rate. In 3 patients who tolerated Fontan operation poorly, converting Fontan to hemi-Fontan abruptly reversed the downhill course. For these patients, the operation was life-saving. Hemi-Fontan operation is safe and well-tolerated, even in infants, provides the advantages of modified Glenn physiology before Fontan operation, and may be especially useful for Fontan takedown after failed Fontan.

(Ann Thorac Surg 1991;51:893–900)

Since its introduction in 1971, the Fontan procedure [1] and its many variants, collectively referred to as orthoterminal correction [2], has become the final goal of surgical treatment of patients with only one functional ventricle. However, certain anatomical and physiological factors militate against successful outcome of a Fontan procedure. These risk factors include very young age, poor systolic or diastolic ventricular function, small or stenotic pulmonary arteries, and elevated pulmonary vascular resistance [3]. The probability that a patient will die after Fontan operation is related to the number and severity of the risk factors associated with the malformation.

For editorial comment, see page 882.

Recently, several methods have been introduced to achieve orthoterminal correction in stages, allowing the circulatory and other systems to adjust gradually to the dramatic physiological changes acutely imposed by the Fontan operation. One such staging procedure is the bidirectional cavopulmonary shunt, which connects the superior vena cava to both pulmonary arteries, thus providing adequate arterial oxygenation without increasing ventricular work, deforming the pulmonary arteries, or risking increase in pulmonary vascular resistance [4]. Cardiac output is not limited by pulmonary blood flow, as it is after a Fontan operation, because much of the systemic venous return goes directly into the ventricle, bypassing the lungs.

A refinement of the bidirectional cavopulmonary shunt is the hemi-Fontan operation [5]. After this procedure, the physiology is that of a bidirectional cavopulmonary shunt, but all aortopulmonary shunts and ventriculopulmonary connections have been interrupted, thus unloading the ventricle of all pulmonary work, and any other anatomical risk factors have been corrected, like reconstruction of pulmonary artery deformities and resection of subaortic obstruction.

Another method of staging orthoterminal correction is the fenestrated Fontan procedure, in which the Fontan operation is completed, but a fenestration a few millimeters in diameter is left in the interatrial septum [6, 7]. Like the bidirectional cavopulmonary shunt, this allows some systemic venous return to bypass the lungs and go directly into the ventricle, thus stabilizing cardiac output.

We report our early experience with the hemi-Fontan operation.

Material and Methods

Data Collection

We reviewed the medical records of all patients at the Medical University of South Carolina undergoing the hemi-Fontan operation from August 1989 to the present. We recorded each patient's age, weight, cardiac malformation, previous operations, and data obtained at echo-

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cardiography and cardiac catheterization. We also recorded operative findings and variables related to postoperative course, including use of cardiotonic drugs, hours to extubation, severity of upper body swelling, intravenous fluid requirements, duration of chest tube drainage, and complications. Follow-up data were reviewed, including subsequent operations and current condition.

Operative Techniques

All hemi-Fontan operations were done with cardiopulmonary bypass and deep hypothermia with or without circulatory arrest (Fig 1). At the time of operation, all other correctable anatomical abnormalities were repaired.

Results

Seventeen hemi-Fontan operations were done in 16 patients: 14 as a primary procedure (group 1) and 3 for takedown of a Fontan operation (group 2).

In group 1, ages ranged from 6 to 69 months (median, 9 months), and 9 patients were less than 1 year of age. Clinical data are summarized in Table 1. Previous operations were as follows: Norwood procedure, 5 patients; central Gore-Tex shunt, 2; Blalock-Taussig shunt, 2; and Blalock-Taussig shunt with atrial septectomy, pulmonary artery band, and coarctation repair with pulmonary artery band, 1 each. Concurrent correction of other anatomical malformations included pulmonary artery reconstruction in 8, shunt ligation in 6, left superior vena cava to left pulmonary artery anastomosis in 2, pulmonary artery band removal in 2, and balloon dilation of residual coarctation in 1. Risk factors for Fontan operation that prompted selection of the hemi-Fontan procedure as well as other complicating features included age less than 1 year in 8, hypoplastic pulmonary arteries in 7, stenotic pulmonary arteries in 5, left ventricular hypertension in 2, aortic insufficiency in 2, left superior vena cava in 3, reactive airway disease in 2, poor ventricular function in 1, prior pulmonary artery band in 2, and pulmonary hypertension in 1. Seven patients (patients 2, 3, 6, 7, 9, 11, and 13) had hypoplastic pulmonary arteries, defined as a pulmonary artery index [8] less than 200 mm^2/m^2; their indices ranged from 118 to 198 mm^2/m^2.

Chest drainage tubes were removed in 1 to 31 days (median, 3 days). Time of endotracheal intubation was 6 hours to 7 days (median, 18 hours). Postoperative days of hospitalization ranged from 6 days to 3 weeks (median, 8 days).

One patient (patient 11) required takedown of the hemi-Fontan operation. This 6-month-old girl with superoinferiorly related ventricles with double-outlet right ventricle and juxtaposition of the atrial appendages had episodic bronchospasm with severe arterial oxygen desaturation postoperatively. Hemodynamic deterioration related to oxygen desaturation occurred in the second postoperative week, and on the 13th postoperative day, the atriopulmonary anastomosis was taken down and an aortopulmonary shunt constructed. Three months later, the patient died, still on a ventilator, with respiratory failure. Autopsy permission was refused. This was the only death in the series.

Important complications occurred in 4 other patients, including subglottic stenosis (patient 13) and transient diaphragmatic paralysis (patient 10), each with prolonged need for endotracheal intubation; residual pulmonary artery stenosis and thrombosis that required reoperation (patient 7); and ventricular fibrillation responding immediately to cardioversion and cardiopulmonary resuscitation (patient 5).

Group 2 comprised 3 desperately ill patients in whom the hemi-Fontan operation was used to take down a recent Fontan procedure because of low cardiac output and high pulmonary artery pressure (Table 2).

Two patients underwent Fontan takedown postoperatively to treat low cardiac output. Patient 17 underwent Fontan operation 6 months after a hemi-Fontan procedure (patient 1 in Table 1). Copious chest tube drainage, up to 1,500 mL a day, led to severe low cardiac output requiring reoperation 8 days postoperatively. He was found to have a peritoneomediastinal fistula that was responsible for the drainage (chest tube draining ascites), and the peritoneal tear was repaired at the time of conversion of Fontan to hemi-Fontan. Patient 16 was in a refractory low output state related to high pulmonary artery pressure, and he underwent conversion to hemi-Fontan 9 days after Fontan procedure. He had diffuse encephalopathy and substantial neurological impairment.

Patient 15 was a 25-month-old boy with a history of prematurity and reactive pulmonary vascular bed. He had poor hemodynamics immediately after the Fontan operation; it was converted to a hemi-Fontan during the same procedure.

All these patients had dramatic hemodynamic improvement immediately after conversion to hemi-Fontan physiology. Postoperative courses were less salutary than those of group 1 patients, but all survived.

Comment

Orthoterminal correction for patients with single ventricle physiology cannot be done safely in small children because of relatively high pulmonary vascular resistance, so palliation is needed for babies with cyanosis due to insufficient pulmonary blood flow. Systemic artery-to-pulmonary artery shunts have been the standard palliation for such cyanotic malformations for several decades [9]. These shunts have been associated with many sequelae that are incremental risk factors for the Fontan operation; for example, pulmonary artery branch stenoses, pulmonary hypertension, and ventricular volume overload with consequent ventricular hypertrophy [10]. Therefore, earlier Fontan operation [11] or palliation by cavopulmonary anastomosis has been proposed [4].

The concept of anastomosis of the superior vena cava to the right pulmonary artery was studied experimentally in the 1950s by Carlon and associates [12] and by Glenn and Patino [13], and shortly thereafter was widely applied clinically. In this procedure, the superior vena cava is connected to the divided end of the right pulmonary

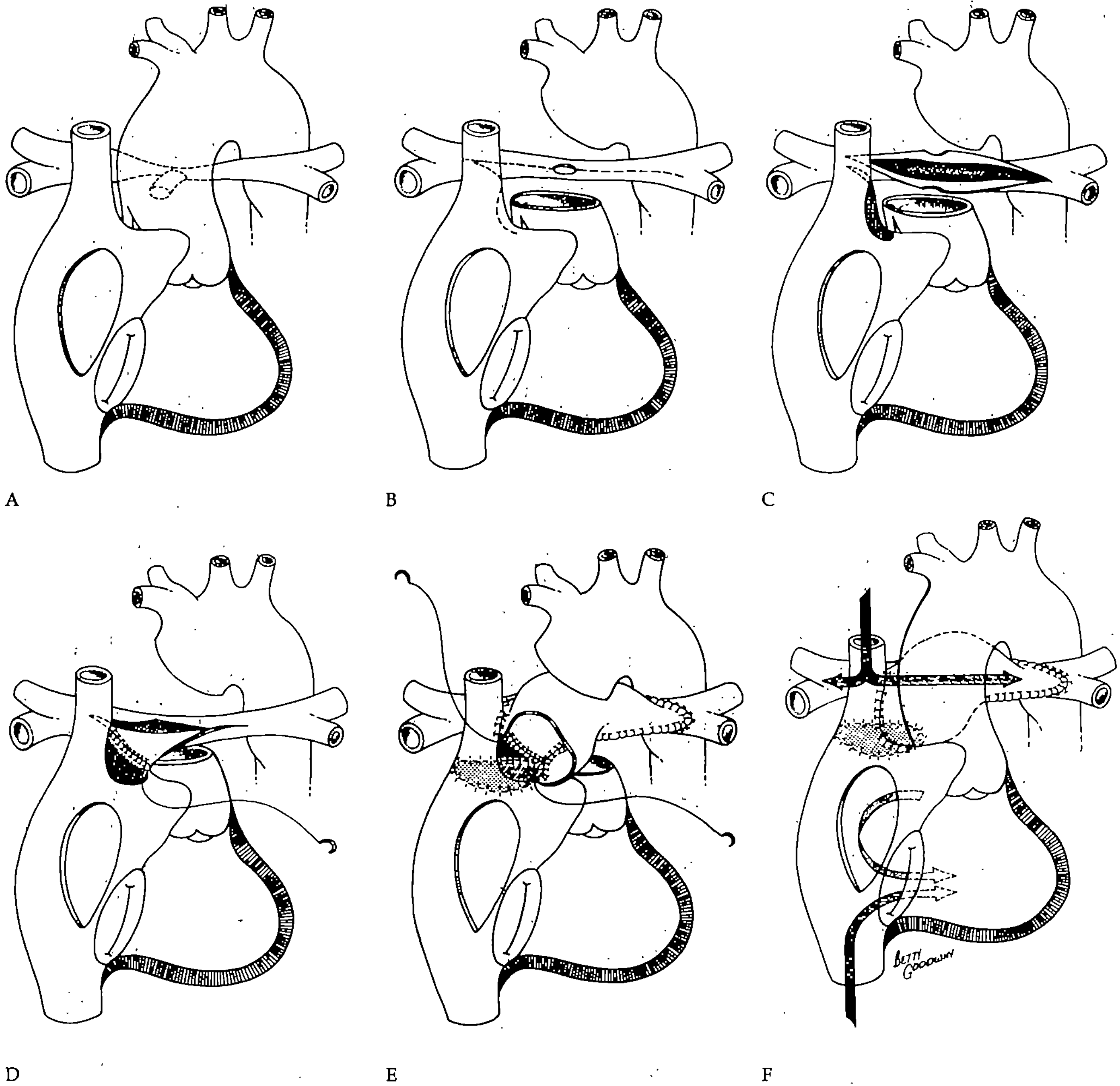

Fig 1. A hemi-Fontan operation is illustrated in a heart with a central Gore-Tex shunt and stenosis of the central pulmonary arteries after Norwood procedure for hypoplastic left heart syndrome. (A) The post-Norwood anatomy is depicted. A large atrial septal defect is present. (B, C) The aorta has been cut away for clarity of illustration. The shunt is removed from the pulmonary artery and oversewn at the aorta. The pulmonary artery is opened from the shunt site into the lower lobe branch on the left, and to a point on the anterior right pulmonary artery immediately posterior to the superior vena cava. The superior vena cava is opened at the cavoatrial junction. The incision spirals cephalad around the medial border of the superior vena cava and ends posteriorly adjacent to the pulmonary arteriotomy. It extends caudally, to the cavoatrial junction, stopping short of the sinus nodal artery to avoid injury. (D) The posterior border of the cavoatrial opening is sutured to the inferior border of the pulmonary arteriotomy with 6-0 polydioxanone suture. A patch of Gore-Tex is sewn into the right atrium immediately below the cavoatrial junction through the open anastomosis, separating the atrium from the cavopulmonary anastomosis. (E) A patch of cryopreserved pulmonary artery homograft is cut to an appropriate shape and is sewn onto the remaining edge of pulmonary artery, starting at its leftward extent, with a continuous suture of 6-0 polypropylene, and this suture line is carried onto the cavoatrial portion of the anastomosis. (F) The patch lies laterally and posteriorly to the aorta. The superior vena caval drainage is into both pulmonary arteries, but the inferior caval drainage mixes with the left atrial return as they both enter the single ventricle. The azygos vein is ligated.

artery. In 1966, Haller and associates [14] reported experimental studies on the bidirectional cavopulmonary shunt, in which the superior vena cava is connected to the undivided pulmonary arteries. This operation was later used by several surgeons [15, 16]. The major advantage of both types of cavopulmonary anastomosis is that the

Table 1. Hemi-Fontan as Primary Procedure (Group 1; n = 14)

Patient No.	PAI (mm^2/m^2)	Age (mo)	Lesion	Int (h)	CT (d)	LOS	Complications	SaO_2
1	226	9	HLHS	16	2	6	Mediastinitis	85%
2	118	69	Mitral atr; pulm atr	10	3	11	. . .	89%
3	198	8	HLHS	18	4	8	. . .	80%
4	343	9	HLHS	6	2	2	. . .	88%
5	245	8	HRHS	23	1.3	7	Cardiac arrest	74%
6	175	15	Mitral atr; sub-PS	18	3	6	Otitis media	74%
7	187	6	HRHS	36	5	16	SVC syndrome; reop × 2	78%
8	326	11	HRHS	16	9	31	. . .	80%
9	193	7	HRHS	16	3	32	Otitis media	80%
10	228	21	HLHS	16	31	51	Paralyzed diaphragm; ventilator dependence	70%
11	122	6	Multiple VSDs; juxtaposition atrial app; TGA with PS; sup-inf vent	NA	NA	NA	PA thrombosis; hemi-Fontan takedown; death	. . .
12	305	60	DILV; SAS; S/P PA band	168	4	15	. . .	80%
13	330	36	Parachute MV; DORV; S/P PAB	16	3	24	Prolonged intubation due to subglottic stenosis	78%
14	157	9	HLHS	48	3	11	. . .	84%

app = appendages; atr = atresia; CT = chest tube duration; DILV = double-inlet left ventricle; DORV = double-outlet right ventricle; HLHS = hypoplastic left heart syndrome; HRHS = hypoplastic right heart syndrome; Int = duration of intubation; LOS = length of stay (postop days); MV = mitral valve; NA = not applicable; PA = pulmonary artery; PAB = pulmonary artery band; PAI = pulmonary artery index; PS = pulmonary stenosis; pulm = pulmonary; SaO_2 = arterial oxygen saturation on room air; SAS = subaortic stenosis; S/P = status post; sup-inf vent = superoinferiorly related ventricles; SVC = superior vena cava; TGA = transposition of the great arteries; VSD = ventricular septal defect.

unsaturated blood flowing through the shunt is not pumped by the ventricle, thus relieving the ventricle of volume work. This contrasts sharply with the large ventricular volume load associated with aortopulmonary shunts.

Pennington and co-workers [17] and DeLeon and colleagues [18] have observed that construction of a classic cavopulmonary shunt before definitive Fontan correction reduces morbidity and mortality at corrective operation. Zellers and associates [19] have shown a favorable effect on pleural drainage and hospital stay in patients undergoing a cavopulmonary shunt before Fontan operation. The bidirectional cavopulmonary anastomosis has been shown to be safe [4] and may confer similar advantages.

The hemi-Fontan operation is physiologically similar to a bidirectional cavopulmonary shunt, but differs in that all sources of pulmonary blood flow other than the superior vena cava and small aortopulmonary collaterals are interrupted, thus unloading the ventricle of volume work as completely as possible. Furthermore, orthoterminal correction is virtually complete, including all necessary pulmonary arterial reconstruction and correction of other

Table 2. Fontan Takedown (Group 2; n = 3)

Patient No.	PAI (mm^2/m^2)	Age (mo)	Lesion	Int (h)	CT (d)	Complications	SaO_2
15	596	25	DILV	16	4	None	80%
16	1100	24	Single ventricle	264	6	Postop encephalopathy; respiratory failure	74%
17	226	14	HLHS	72	7	Sinusitis and right pneumothorax	78%

Abbreviations same as in Table 1.

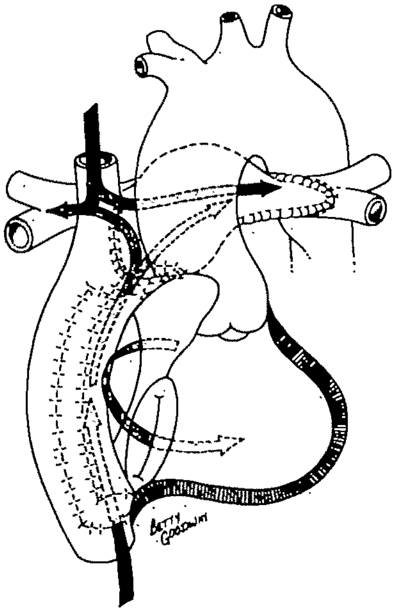

Fig 2. The completion Fontan operation is accomplished by opening the right atrium, removing the atriopulmonary patch, and implanting into the right atrium a baffle from the inferior vena cava to the atriopulmonary anastomosis. Thus, all systemic venous return is directed to the pulmonary capillary bed, and all pulmonary venous return is directed to the aorta.

associated lesions, except for a patch that separates the right atrium from the atriopulmonary anastomosis. Thus, the subsequent Fontan operation requires only repositioning of the intraatrial patch to separate the systemic and pulmonary circulations (Fig 2).

After a Fontan operation, all systemic venous return must flow through the pulmonary capillary bed, so cardiac output is determined by pulmonary blood flow. Elevation of pulmonary vascular resistance, due to such factors as pulmonary arteriolar spasm, pulmonary interstitial edema, or high left atrial pressure, will lead to decreased cardiac output. Although potentially reversible, such changes may be fatal because of their effect on cardiac output in the postoperative patient. After a hemi-Fontan operation or bidirectional cavopulmonary shunt, however, the cardiac output is not entirely dependent on pulmonary blood flow, because the inferior vena caval return bypasses the lungs and goes directly into the ventricle. Thus a stable cardiac output is achieved at the cost of moderate cyanosis. This fundamental difference leads to the expectation that the postoperative course after hemi-Fontan will be substantially smoother than after Fontan operation.

Our series confirms this expectation. The hemi-Fontan operation done as a preliminary stage before Fontan completion is relatively safe. Despite the fact that most children in group 1 would not have been candidates for a Fontan operation due to age or substantial risk factors, most did well: endotracheal extubation, chest tube removal, and hospital discharge were accomplished early in the majority of patients. Palliation was good, oxygen saturation averaging 80%. Complications that prolonged postoperative management were seen in 3 children. The only death occurred in a child with refractory respiratory failure of unclear cause.

Our study does not answer an important question: does a preliminary hemi-Fontan operation actually decrease morbidity and mortality after the subsequent completion Fontan operation? Five of the 13 children in group 1 have undergone Fontan operation, too small a number to answer this question definitively. At the age of 14 months, patient 1 underwent completion Fontan operation which had to be converted back to hemi-Fontan 7 days postoperatively because of low cardiac output caused by loss of large amounts of ascitic fluid. Patient 7 was 13 months old when she had Fontan operation. Low cardiac output led to fenestration of the intraatrial baffle in the catheterization laboratory on the sixth postoperative day. She had immediate marked hemodynamic improvement after this maneuver but then suffered respiratory failure and sinusitis, requiring prolonged intensive care. She was discharged from the hospital 10 weeks postoperatively. The 3 other children (patient 6 at age 21 months, patient 2 at age 76 months, and patient 3 at age 14 months) did well after Fontan operation: their chest tubes were removed 7, 13, and 10 days after operation, and they were discharged 10, 20, and 14 days after operation, respectively. Patient 6 had a cerebrovascular accident, and has residual right hemiparesis. It is of interest to note that patient 2 had the smallest pulmonary artery index (118 mm^2/m^2) of the entire series.

Our group 2 demonstrates that the hemi-Fontan operation is particularly useful in a postoperative Fontan patient who has high pulmonary artery pressure and inadequate cardiac output. Taking down a Fontan operation has been associated in previous reports with a high mortality rate [20]. Our 3 patients improved dramatically after operative conversion to hemi-Fontan physiology. All survived Fontan takedown, and will be reevaluated in the future as candidates for completion operation.

During pulmonary artery reconstruction, we have found pulmonary artery cryopreserved homograft to be technically superior to autogenous or bovine pericardium and to Dacron or Gore-Tex patches because of its compliance and handling characteristics. We use it routinely for all such reconstructions.

Patients with single ventricle who may benefit from this operation can be broadly categorized into three groups. The first category comprises children who are candidates for a Fontan operation but are at high risk; for example, patients with high pulmonary artery pressure due to large ventricular volume overload, high ventricular end-diastolic pressure, severe but correctable pulmonary artery deformity, ventricular hypertrophy due to subaortic obstruction, marginal pulmonary vascular resistance, or a combination of risk factors. This group also includes children who need palliation of cyanosis, are older than 3 to 4 months, but are too young to undergo Fontan operation safely (less than about a year old).

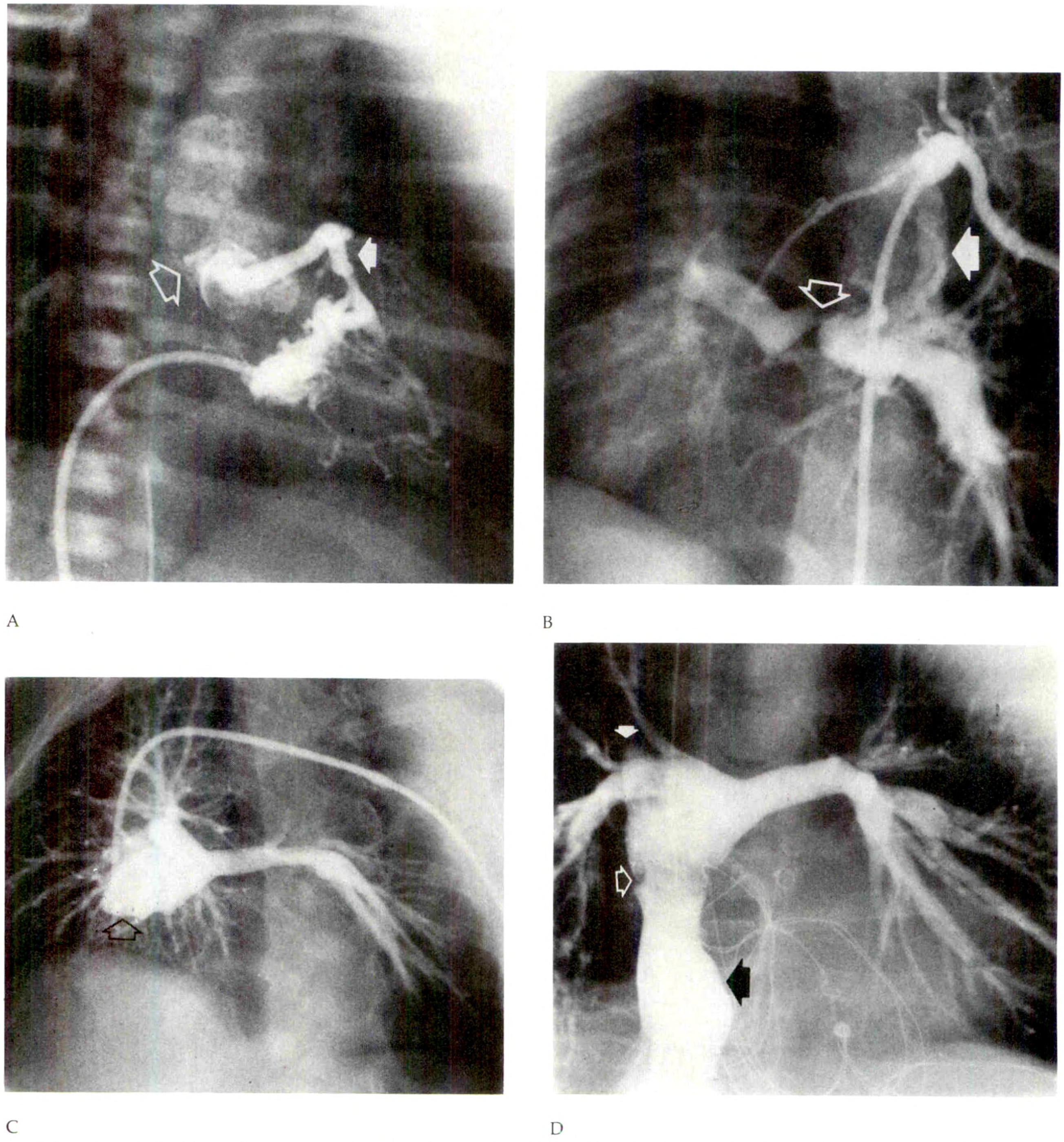

Fig 3. Angiograms of a girl (patient 7) with pulmonary atresia with intact ventricular septum with ventriculocoronary connections (hypoplastic right heart syndrome). (A) Patient is a neonate. Right anterior oblique projection of a right ventriculogram demonstrates hypoplastic right ventricle connected to the coronary circulation by way of several fistulas (sinusoids), including a large anterior fistula (white arrow) *communicating with the left coronary artery. The aortic root* (open arrow) *fills through the coronary arteries. (B) Patient is 6 months old; Blalock-Taussig shunt was done in newborn period. Left anterior oblique projection of a left subclavian arteriogram demonstrates the left modified Blalock-Taussig shunt* (white arrow) *filling the left pulmonary artery. There is severe stenosis of the left pulmonary artery* (open arrow) *at the site of the original ductus arteriosus, proximal to the shunt. (C) Patient now 12 months old, having had a hemi-Fontan operation at age 8 months. Left anterior oblique projection of a pulmonary arteriogram shows a large anastomosis with no stenoses of the branch pulmonary arteries. The right atrial atriopulmonary patch is indicated* (arrow)*. (D) Patient, 14 months old, has undergone completion Fontan procedure. Anteroposterior projection with injection of contrast medium into intraatrial baffle* (black arrow) *shows flow from inferior vena cava through atriopulmonary anastomosis into pulmonary arteries. The site where the atriopulmonary patch was excised is visible as a slight defect representing scar tissue at the excision site* (open arrow)*. The superior vena cava is also barely visualized* (white arrow)*.*

The second category comprises children whose physiology may especially benefit from early unloading of ventricular volume, such as those who have pulmonary atresia with intact ventricular septum with compromised coronary artery circulation. Although reasonable long-term survival of these patients has been occasionally reported [21], we have had dismal results in treating this lesion [22]. We have therefore embarked on a program of early hemi-Fontan operation (before the age of 6 months) for these children, followed by Fontan operation in 6 months to a year. Four of 5 patients we diagnosed in the last year have survived through hemi-Fontan, and one has had successful completion of a Fontan operation (patient 7, Fig 3).

Finally, a class of patients who may benefit greatly from this operation contains children early after Fontan operation who are experiencing low cardiac output with high pulmonary artery pressure. The reversal of downhill course in our 3 patients who had this operation was so dramatic that it suggested hemi-Fontan may be the operation of choice for patients with failing Fontan physiology. We had 1 other patient (patient 7) with low cardiac output after Fontan, however, who responded well to fenestration of the interatrial patch in the catheterization laboratory, already described. Either of these maneuvers may be useful in such a patient. Hemi-Fontan reduces the inferior vena caval pressure to left atrial level, whereas fenestration leaves that pressure at pulmonary artery level; for a moribund patient, this may be a decisive advantage of the hemi-Fontan.

It is clear that the hemi-Fontan operation is a safe, effective, and well-tolerated means of palliating children with single ventricle who have substantial risk factors for Fontan operation. Correction of associated risk factors during that procedure may simplify the eventual Fontan operation, which can be accomplished by simply realigning the intraatrial patch. The hemi-Fontan may be especially valuable to take down failed Fontan operations. More data are needed to define precise roles for each of the proposed staging procedures, and to document the improvement we hope to observe in ultimate outcome of Fontan correction for children with single ventricle.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8.
2. Sade RM. Orthoterminal correction of congenital cardiovascular defects. Ann Thorac Surg 1975;19:105–7.
3. Kirklin JK, Blackstone EH, Kirklin JW, Pacifico AD, Bargeron LM Jr. The Fontan operation. Ventricular hypertrophy, age, and date of operation as risk factors. J Thorac Cardiovasc Surg 1986;92:1049–64.
4. Lamberti JJ, Spicer RL, Waldman JD, et al. The bidirectional cavopulmonary shunt. J Thorac Cardiovasc Surg 1990;100:22–30.
5. Jacobs ML, Norwood WI, Hypoplastic left heart syndrome. In: Jacobs M, Norwood WI, eds. Current issues in pediatric heart surgery. Stoneham: Butterworth (in press).
6. Laks H, Haas GS, Pearl JM, et al. The use of an adjustable intraatrial communication in patients undergoing the Fontan and other definitive procedures. Circulation 1988;78(Suppl 2):357.
7. Bridges ND, Lock JE, Castaneda AR. Fontan repair with baffle fenestration and subsequent transcatheter closure in high risk patients. J Am Coll Cardiol 1990;15:203A.
8. Nakata S, Imai Y, Takanashi Y, et al. A new method for the quantitative standardization of cross-sectional areas of the pulmonary arteries in congenital heart diseases with decreased pulmonary blood flow. J Thorac Cardiovasc Surg 1984;88:610–9.
9. Sade RM, Fyfe DA. Tricuspid atresia. In: Sabiston DC, Spencer FC, eds. Gibbon's surgery of the chest. Philadelphia: W.B. Saunders, 1990:1461–84.
10. Sade RM. Surgical options in univentricular atrioventricular connection. In: Jacobs M, Norwood WI, eds. Current issues in pediatric heart surgery. Stoneham: Butterworth (in press).
11. Mietus-Snyder M, Lang P, Mayer JE, Jonas RA, Castaneda AR, Lock JE. Childhood systemic–pulmonary shunts: subsequent suitability for Fontan operation. Circulation 1987; 76(Suppl 3, Pt 2):39–44.
12. Carlon CA, Mondini PG, DeMarchi R. Surgical treatment of some cardiovascular diseases (a new vascular anastomosis). J Int Coll Surg 1951;16:1–10.
13. Glenn WWL, Patino JF. Circulatory bypass of the right heart. I. Preliminary observations on the direct delivery of vena caval blood into the pulmonary arterial circulation. Azygos vein–pulmonary artery shunt. Yale J Biol Med 1954;27:147.
14. Haller JA, Adkins JC, Worthington J, et al. Experimental studies on permanent bypass of the right heart. Surgery 1966;59:1128.
15. Azzolina G, Eufrate S, Pensa P. Tricuspid atresia. Experience in surgical management with a modified cavopulmonary anastomosis. Thorax 1972;27:111–5.
16. Hopkins RA, Armstrong BE, Serwer GA, Peterson RJ, Oldham HN Jr. Physiological rationale for a bidirectional cavopulmonary shunt: a versatile complement to the Fontan principle. J Thorac Cardiovasc Surg 1985;90:391.
17. Pennington DG, Nouri S, Ho J, et al. Glenn shunt: long-term results and current role in congenital heart operations. Ann Thorac Surg 1981;31:532–8.
18. DeLeon SY, Idriss FS, Ilbawi MN, et al. The role of the Glenn shunt in patients undergoing the Fontan operation. J Thorac Cardiovasc Surg 1983;85:669–77.
19. Zellers TM, Driscoll DJ, Humes RA, Feldt RH, Puga FJ, Danielson GK. Glenn shunt: effect on pleural drainage after modified Fontan operation. J Thorac Cardiovasc Surg 1989; 98:725–9.
20. DeLeon SY, Ilbawi MN, Idriss FS, et al. Persistent low cardiac output after the Fontan operation. Should takedown be considered? J Thorac Cardiovasc Surg 1986;92:402–6.
21. Hawkins JA, Thorne JK, Boucek MM, et al. Early and late results in pulmonary atresia and intact ventricular septum. J Thorac Cardiovasc Surg 1990;100:492–7.
22. Sioufi S, Sade R, Crawford F, Gillette P, Fyfe D, Taylor A. Myocardial sinusoids in pulmonary atresia with intact ventricular septum. In: Doyle EF, Engle MA, Gersony WM, Rashkind WJ, Talner NS, eds. Second World Congress of Pediatric Cardiology [Abstracts]. New York: Springer-Verlag, 1985:146.

DISCUSSION

DR TIMOTHY J. GARDNER (Baltimore, MD): I congratulate you on an excellent paper. The anatomical and surgical illustrations were superb and your points of emphasis were very appropriate.

It is worth recalling that in the evolution of the surgical treatment of conditions such as single ventricle and tricuspid atresia, Alex Haller did some of the important and innovative early work in this field and, in fact, he was the first to describe an experimental preparation that represents what we now refer to as a bidirectional Glenn shunt.

Glenn Pennington was also very interested in the issue of surgical staging when using Fontan's repair and several years ago he presented a paper describing the course of patients who had classic Glenn shunts followed by the Fontan repair. Many of us were interested in that concept, but found that the conventional Glenn shunt, that is, a superior vena cava-to-right pulmonary artery shunt, was not a reliable first step. The present approach, or the use of a bidirectional Glenn shunt, which is the specific approach that we have taken, has made the treatment of single ventricle and other variants requiring a Fontan repair much safer.

Our own bias is that the bidirectional Glenn shunt, which is accomplished simply by transecting the superior vena cava and anastomosing it to the pulmonary artery, is a simpler option than the one here. Both approaches obviously are quite acceptable and as your results are so outstanding, there can be no arguing with your approach. Because we do perform the bidirectional Glenn shunt on bypass, we can eliminate any troublesome central shunts at that time and do any required pulmonary artery construction concurrently, as with your approach.

The most important point to be taken from your outstanding results, I believe, is that with such a first-stage procedure, one can successfully back out of a Fontan repair if it is clear that the patient cannot tolerate the complete redirection of systemic venous return to the lungs. One is able to do the same thing if there is an existing bidirectional Glenn shunt in place, and in either case the surgical management of these complex patients should be greatly improved.

DR CONSTANTINE MAVROUDIS (Chicago, IL): That was a very nicely presented paper on a very difficult set of patients. I have a few comments to make and also some questions to ask.

In these very difficult patients, completion of the entire Fontan operation many times leads to emergent reoperation for Fontan takedown and systemic-to-pulmonary artery shunt. A propos to the partial Fontan, we performed this operation along with aortic reconstruction in a 30-day-old neonate with hypoplastic left heart syndrome. Our thought was that after 30 days the pulmonary hypertension of the newborn may be more treatable with direct nitroglycerin infusion into the pulmonary artery along with prostaglandin E_1. We reasoned that this would allow the bidirectional Glenn shunt to allow enough blood for adequate oxygenation. The child survived for 3 days and died of pulmonary hypertension and cyanosis. Until we can alter the pulmonary hypertensive events in the newborn, this is not something one can use early on.

My other comments involve the partial Fontan that you have described and also the so-called fenestrated Fontan that we have been using. That is to say, we perform the Fontan and leave a small hole in the atrial septation. We have performed this in children as young as 1 year of age. A hole of varying degree between 2.7 and 5 mm is created in the atrial septation and is closed at a later date with a clam shell device after the transient rise in pulmonary hypertension abates. That has been working very well and may represent an intermediate stage for your patients. Perhaps in some patients a full Fontan with a fenestration can be accomplished with subsequent transcutaneous clam shell closure at 1 year of age. These issues, however, will become clear as the story becomes unfolded.

The other issue that I want to explore is the use of jet ventilation for these patients. The group at the University of Michigan has been testing this technology recently with encouraging results. Have you used jet ventilation? My other question relates to anatomical reconstruction. Many surgeons use the caval pulmonary artery anastomosis. That is to say, the superior vena cava is divided and end-to-end anastomoses are accomplished to the superior and inferior portion of the right pulmonary artery. One can easily enlarge the anastomosis by using a piece of prosthetic patch for the inferior superior vena cava to right pulmonary artery anastomosis if necessary. Have you been using this type of repair?

This is truly an exciting field. I congratulate you on a very nicely presented paper.

DR DOUVILLE: We have not used high-frequency ventilation in these children. We believe that an important advantage of the hemi-Fontan over the bidirectional Glenn shunt is that the completion Fontan simply requires removal of the Gore-Tex patch separating the atrium from the atriopulmonary anastomosis and insertion of a baffle from the inferior vena cava to the atriopulmonary anastomosis. Thus far, we have been satisfied with the technical ease with which this has been accomplished. Furthermore, the hemi-Fontan removes all intracardiac and extracardiac left-to-right shunts, thus completely unloading the ventricle and allowing establishment of optimal ventricular function before completion Fontan.

DR DONALD C. WATSON, JR (Memphis, TN): This is an excellent paper and I think, as has been previously commented, marks a new era in the treatment of congenital heart disease. We also have adopted this principle, although we have chosen to use the bidirectional Glenn shunt. We have been able to do about half of these off bypass simply by cannulating the superior vena cava superiorly and the right atrium inferiorly and isolating the vascular portions for the anastomosis you want to create. This avoids the problems of hemodilution with cardiopulmonary bypass. Because these patients are still hypoxemic after operation, one does not have to go through a hemoconcentrating transition period.

I would like to ask one question, and that is regarding the criteria for when you convert these hemi-Fontans or bidirectional Glenn shunts into completion Fontans. With this postoperative anatomy one has a little more than one third of the cardic output going to the pulmonary circulation. Our previous criteria have been pulmonary pressure and pulmonary resistance related. We may be on the forefront of learning more about the limits of objective criteria for completion Fontan. I would like to hear your thoughts on how we are going to make the decision for a completion Fontan in the future.

DR DOUVILLE: We are still defining the timing of completion Fontan. We generally wait 6 to 12 months after hemi-Fontan, based on the patient's clinical course. Most of these patients are still far from ideal Fontan candidates, so we are also evaluating the role of fenestration; many hemi-Fontan patients may require a fenestration at the time of completion Fontan.

Are Sutures Better Than Staples for Closing Bronchi and Pulmonary Vessels?

Geoffrey M. Graeber, MD, Joseph J. H. Collins, Jr, James L. DeShong, BS, and Gordon F. Murray, MD

Department of Surgery, West Virginia University, Health Sciences Center North, Morgantown, West Virginia

Little is known about the strength of suture lines and stapled closures of the bronchus, pulmonary arteries, and pulmonary veins. This experiment tested and compared the hydrostatic leakage point of each of these structures when closed by either sutures or staples. Fourteen fresh mature porcine cadavers and 8 human cadavers of age greater than 50 years were studied to determine whether the pig could be used as an appropriate model for future in vivo studies. Cadavers were selected so that closures depended only on the material used and not on any clot reinforcing the closure lines. The results of the study suggest that staple closure of the pulmonary artery and the main bronchus is as secure as suture closure. Pulmonary veins leak at a lower pressure when closed with staples; however, this pressure far exceeds physiological pressures in the left atrium. The data also suggest that the pig is an appropriate model for approximating conditions found in patients and is a good model for chronic studies comparing suture and staple closures.

(Ann Thorac Surg 1991;51:901–5)

The Russians were the first to use stapling devices in pulmonary resection to close cut lung and secure bronchial stumps [1, 2]. In 1959 and 1964, after visits to the Soviet Union, Ravitch and colleagues [3, 4] presented these concepts in North America. A few surgeons recognized the advantages of stapled bronchial closure early when the techniques were being developed and refined [5–8]. Both clinical and experimental trials [3, 9, 10] have documented that fewer bronchopleural fistulas occur when improved stapling devices are used to secure bronchial stumps.

The efficacy of the stapled closure depends on the type of stapling instrument employed. Devices that place at least two parallel, overlapping rows of metallic staples transversely across the bronchus are superior to sutured closures and to devices that insert staples parallel to the long axis of the transected bronchus [11, 12]. Hinged devices are more likely to foster development of bronchopleural fistulas than are stapling instruments with two jaws that close in parallel [13]. The concept of parallel jaw closure has been adapted to most devices available today whether they employ two or three rows of metallic staples. The security of metallic staple lines is due partially, according to some authors [14], to the fact that the staples are very inert and cause little inflammation in the bronchial stump.

Less has been written concerning staple closure of the pulmonary artery and pulmonary veins. There are a few anecdotal reports and some clinical experiences attesting to the security of metallic suture lines placed on pulmonary vessels [4, 11].

We undertook the following study to investigate the immediate leakage pressures of closures in the bronchi, pulmonary arteries, and pulmonary veins in fresh human cadavers in the age range when pulmonary resection is most frequent. Cadavers were selected mainly because we did not wish to have clot reinforce our closure lines in any way. Staple closures were compared with suture closures in each cadaver. We also chose to compare the leakage pressures of the closures in human cadavers with those in fresh porcine cadavers to establish whether the pig would be a suitable model for chronic studies to investigate the long-term changes that occur in the closure of the three structures after operation.

Material and Methods

Eight cadavers of humans 50 years old or older (average age, 56 years; range, 50 to 62 years) that were donated to the West Virginia University School of Medicine within 24 hours of death served as the human study group. There were 6 men and 2 women. The animal group consisted of 14 adult pigs that were killed for meat processing (weight range, 50 to 70 kg).

All specimens were dissected so that the heart, both lungs, the great vessels, and surrounding tissues remained en bloc. All bronchi, pulmonary arteries, and pulmonary veins were cleaned of areolar tissue, washed to remove any remaining blood and clot, and transected so that they could be studied as isolated entities.

Even-numbered subjects had staples placed on the structures first. After the leakage pressure was tested, the staple lines were resected, and a suture closure was conducted. Odd-numbered subjects had suture closure

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first, were tested, had the closure line resected, and then had staples applied to each structure for the final test.

Closures were appropriate for each structure. Main bronchi had suture closures constructed with 3-0 silk sutures placed individually and tied to effect secure approximation of the cut edges. A 3M PI-55 stapling device (3M, St. Paul, MN) was used to close each bronchus with a staggered, parallel double row of 3.5-mm staples placed transversely to the long axis of the bronchus. After proximal cannulation of the bronchus, each closure was inflated with air to 40 mm Hg to assure competence. This procedure was conducted to ensure that each bronchial closure would be tested as it is clinically in our practice.

Each main pulmonary artery had a double row of sutures placed for closure. The first layer was a row of 4-0 polypropylene horizontal mattress sutures placed 4 mm proximal to the cut edges. A second layer of running 4-0 polypropylene sutures secured the distal edges of the closure. Staple closures of the pulmonary arteries were conducted using the same instrument as in the bronchial closures. Two rows of 3.5-mm metallic vascular staples were placed in a parallel, staggered pattern transversely to the long axis of the pulmonary artery. None of the arterial closures were stressed in any way before testing.

The pulmonary veins were treated in a manner similar to the pulmonary arteries. Suture closure was conducted with two layers of running 7-0 polypropylene. A horizontal mattress layer was placed first 4 mm from the cut edges. The second running stitch secured the end of the anastomosis. Staple closures were conducted with 3M PI-15 2.5-mm vascular staples. Two parallel, overlapping rows of metallic staples were placed by the cartridge to secure closure. The closures were not stressed in any way before testing.

Leakage pressures of all closures were tested on the apparatus shown in Figure 1. A 50-mL syringe filled with a solution of 1 part methylene blue to 50 parts saline solution was connected by pressure tubing to a transducer (model 075103; Medex, Mountain View, CA). The pressures in the system were monitored visually (Space Labs monitor model 90623A; Redmond, WA) and permanent recordings made (Space Labs recorder model 90651). The tubing exiting from the transducer ran to a stopcock, affixed to which was a Titus needle or a tubular cannula. The size of cannula selected varied with the size of the bronchus or vessel to be tested.

Each structure was tied to the cannula before testing. All air was evacuated from the entire system. Pressure was increased until there was leakage of blue dye at the closure of the structure being tested. When leakage occurred, the closure was inspected to determine the cause. Staple and suture lines were inspected to confirm that they had remained intact and functioning.

Results were tabulated and compared between suture and staple closures for pressures needed to cause leakage. Wilcoxon's signed-rank test was applied to the data to determine whether significant differences existed between methodologies [15]. Significance was achieved when a p level of less than 0.05 arose for any set of compared values.

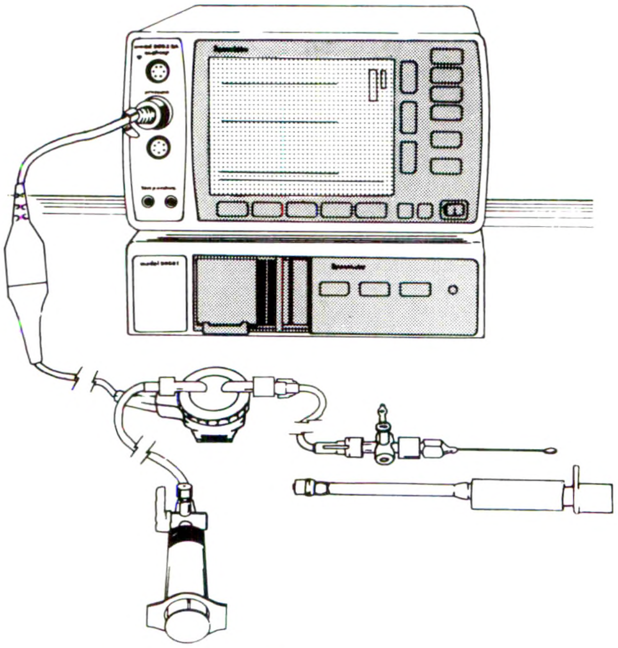

Fig 1. The testing apparatus. The injecting syringe is connected to a transducer by pressure tubing. The transducer readings appear on a visual monitor and are recorded simultaneously. Shown to the right below the recording device are a Titus needle and a modified cannula. The internal diameter of the structure being tested dictated the size of the pressure cannula used.

Results

The pressure required to cause leakage in any of the bronchial closures was nearly 300 mm Hg in all groups (Fig 2). No difference was noted between the sutured and stapled bronchial closures in the human cadavers. The slight difference between closures seen in the porcine model favored staples but did not achieve significance. There was no significant difference between the pressures necessary to cause leakage in the human or porcine groups. Leakage in all closures occurred first at the suture or staple line.

The pressure required to cause leakage of the pulmonary artery closures was 250 mm Hg (Fig 3). There was no

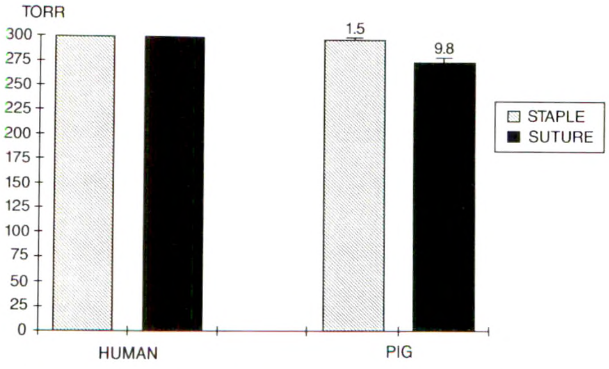

Fig 2. Pressures required to cause leakage in bronchial stump closures. Standard error of the mean for each group is above each bar.

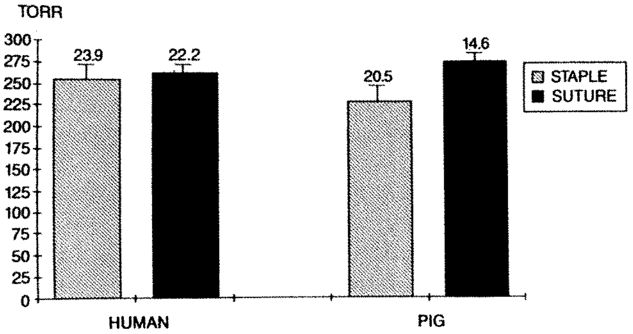

Fig 3. Pressures required to cause leakage in pulmonary artery closures. Standard error of the mean for each group is above each bar.

discernible difference between the sutured and stapled closures in the human cadavers. In the porcine arterial closures, the slight difference favoring suture closure did not achieve significance. No significant difference was found between the different closures in the porcine or human groups. Leakage occurred first at the lines of closure with blue fluid seeping through the tissues around the sutures or staples. Flow through the lumen did not occur until further pressure was applied.

Interesting differences existed in the pressure required to cause leakage of pulmonary vein closures, even though all pressures exceeded normal left atrial pressures (Fig 4). The suture closure was significantly better in human cadavers. Although suture closure appeared better in pigs, it did not achieve significance. Suture closures in the human and porcine models had virtually identical leakage points.

Comments

Closures of each structure were conducted as closely as possible to the methods used in our clinical practice, as we wished to evaluate the leakage (failure) pressure of the respective structures. We varied in only two closures for specific reasons. First, we used 3-0 silk instead of absorbable material to close the bronchus because of lower cost. The size of the suture was identical to that used in our clinical practice. This closure technique was proved efficacious in one large clinical study [16] with a bronchopleural fistula rate of only 2.7%. Second, before this study, we regularly closed the pulmonary veins with a double layer of 5-0 or 6-0 polypropylene sutures. In this experiment we used 7-0, as we wished to make very small holes in the veins because no blood was available to clot on the suture line or areolar tissue near the closure.

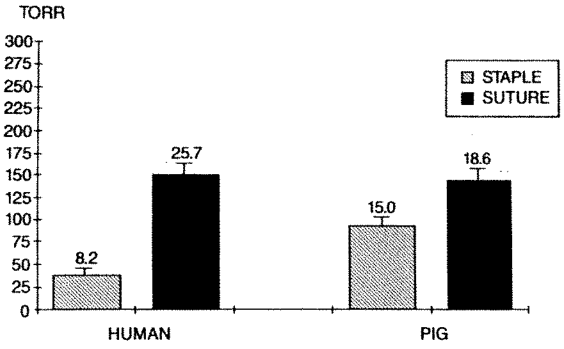

Fig 4. Results of testing pulmonary vein closures. Standard error of the mean for each group is above each bar.

The bronchial closures were secure to nearly 300 mm Hg in all groups. We chose to use 3.5-mm staples to see if they held as securely as 4.8-mm staples. Our tests suggest that they hold as well under the conditions stated. In a previously published study [17], the average mean intraluminal bronchial pressure during vigorous coughing in young adult men was reported as 200 mm Hg. Hence, we are reasonably sure that either sutures or staples, when placed properly using good surgical technique, will achieve a strong, competent closure.

The arterial closures were secure to 225 to 250 mm Hg without leakage. Such pressures exceed any physiological pressure ever generated in the pulmonary artery. Closure of the pulmonary artery when performed properly with either staples or sutures should be quite secure.

The difference in the leakage pressures observed in the pulmonary veins can be attributed to several factors. The staples employed were designed to encompass securely 1.0 to 1.5 mm of tissue. We found that the thickness of the pulmonary veins was less than 1.0 mm in the human cadavers. The pulmonary veins in the pigs were slightly thicker than those in the human cadavers. Hence, the staples performed better on the porcine veins. Suture closure of the pulmonary veins in the porcine and human cadavers leaked only when the tissue started to recede from the closure material under pressure.

How has this information altered our clinical practice? The main difference is in our closure of the pulmonary vessels, as we have routinely used stapling instruments to achieve secure bronchial closures. We now employ stapling instruments on the main pulmonary artery and its major branches. Smaller arterial branches encountered during some lobectomies and segmentectomies are still suture ligated because the diameter of the vessels would allow placement of only a few staples. We close all lobar pulmonary veins with stapling instruments but endeavor to incorporate areolar tissue and the edge of the pericardium in our stapled closure lines. Segmental veins are still suture ligated for reasons of cost and efficiency. Closure of calcific bronchi when found in the cadavers was secure when staples were used. This finding correlated with our clinical experience, in which we routinely use staples on all bronchial closures, including those on calcified bronchi.

We thank Minnesota Mining and Manufacturing (3M), St. Paul, MN, for contributing the stapling devices and the cartridges used in this study. We also thank Ms Carol DeShong for assistance in manuscript preparation, Ms Kay Beamer for laboratory assistance, Mrs Pat Wilbur for photography, Mrs Bonnie Starkey for illustrations, and Jerry Hobbs, PhD, our statistician.

References

1. Amosov NM. Tudoresectio bronchus es ervarrogeppel. Tuberkulozis (Budapest) 1960;12:353-7.
2. Amosov NM, Berezovsky KK. Pulmonary resection with mechanical suture. J Thorac Cardiovasc Surg 1961;41:325-35.
3. Ravitch MM, Brown IW, Daviglus GF. Experimental and clinical use of the Soviet bronchus stapling instrument. Surgery 1959;46:97-108.
4. Ravitch MM, Steichen FM, Fishbein RH, Knowles PW, Weil P. Clinical experiences with the Soviet mechanical bronchus stapler (UKB-25). J Thorac Cardiovasc Surg 1964;47:446-54.
5. Androsov PI. On instruments for suturing the bronchial stump (UKB-25 and -16). Clin Surg (Tokyo) 1962;17:976-80.
6. Goldman A. An evaluation of automatic suture with UKL-60 and UKL-40 devices by pulmonary resection. Dis Chest 1964;46:29-36.
7. Kreszler P. The mechanical suture with UKL-40 and UKL-60 in pulmonary surgery. Dis Chest 1969;56:383-91.
8. Rzepsecki W, Birecka A, Goralczyk J. Mechanical suture with metallic material in resection of pulmonary tissue (the UKL-60 apparatus). Am Rev Respir Dis 1962;86:798-809.
9. Hood RM, Kirksey TD, Calhoun JH, Arnold HS, Tate RS. The use of automatic stapling devices in pulmonary resection. Ann Thorac Surg 1973;16:85-98.
10. Dart CH Jr, Scott SM, Takaro T. Six-year clinical experience using automatic stapling devices for lung resections. Ann Thorac Surg 1970;9:535-50.
11. Betts RH, Takaro T. Use of a lung stapler in pulmonary resection. Ann Thorac Surg 1965;1:197-202.
12. Forrester-Wood CP. Bronchopleural fistula following pneumonectomy for carcinoma of the bronchus: mechanical stapling versus hand suturing. J Thorac Cardiovasc Surg 1980;80:406-9.
13. Hakim M, Milstein BB. The role of automatic staplers in the aetiology of bronchopleural fistula. Thorax 1985;40:27-31.
14. Scott RN, Faraci RP, Hough A, Chretien PB. Bronchial stump closure techniques following pneumonectomy: a serial comparative study. Ann Surg 1976;184:205-11.
15. Campbell RC. Statistics for biologists. New York: Cambridge University Press, 1967:38.
16. Williams NS, Lewis CT. Bronchopleural fistula: a review of 86 cases. Br J Surg 1976;63:520-2.
17. Goffi FS, Gonçalves EL. Closure of bronchial stump after pneumonectomy: comparison of some techniques through evaluation of tensile strength of suture. Surgery 1957;42: 511-20.

DISCUSSION

DR KAMAL A. MANSOUR (Atlanta, GA): I congratulate Dr Graeber for a very nice piece of work that reaffirms the safety of the stapling devices in pulmonary resections.

I have two questions. You used human cadavers in your study, and I thought the bronchial healing depends on a good blood supply. Did you take this into consideration? Second, we know anatomically that the pulmonary artery is an elastic artery, whereas the pulmonary vein is a muscular vessel. It incorporates a good part of the cardiac muscle fiber in its wall, so it is tougher than the artery. Clinically we know that, and histologically we know that. Why did you use 7-0 Prolene for the vein, which is stronger, and 4-0 Prolene for the artery, which is weaker?

DR GRAEBER: We designed this study simply because we could not find anything in the literature that told us what the actual tissue tensile strength was to secure these structures immediately if we closed them with sutures or with staples. That is why we took the cadaver specimens. We wanted no clot or areolar tissue on the structures to reinforce our closure lines.

The long-term studies that have been done on closures obviously recognize and confirm that a good blood supply is essential for bronchial healing. In our clinical practice, we preserve the bronchial blood supply. This study was designed simply to look at the pressures these tissues could endure and remain closed in the immediate postoperative period. Hence, we looked at the walls without areolar tissue and without blood vessels.

Regarding the suture selected for the pulmonary vein, we used 7-0 polypropylene because we found that in older patients, the walls of the veins, like the walls of the arteries and bronchi, become fairly attenuated. When we cleaned them of areolar tissue, they were exceedingly thin. Hence, we wanted to use the smallest possible needles so that we would not be creating artificially large holes. We use 4-0 polypropylene clinically, both for the artery and for the vein.

DR MANSOUR: Why not use 7-0 Prolene for the artery as well?

DR GRAEBER: We thought that the artery had more elastic tissue in it and would probably contract down around the sutures better.

DR HARVEY W. BENDER (Nashville, TN): I have three comments. First, I am a little concerned about the whole premise of the study. I believe that it is not the material used that determines whether or not a suture line leaks, but rather that leakage is more frequently due to the placement of the sutures or the placement of the staples. In addition, you have set up a situation in which you are dealing with pressures that are far in excess of what you will see clinically.

Second, I am bothered a little bit by your implication that there are fewer leaks from bronchial closure with staples than with sutures. I think that depends on which articles you pull from the literature. There are certainly reports of large numbers of pulmonary resections with a very low incidence of bronchial leak that have been suture closed.

Third, the title of your presentation was a question, and I did not hear the answer.

DR GRAEBER: Thank you very much, Dr Bender. I will answer the second point first. Based on this study and what we have seen clinically, we think that staples are just as efficacious as sutures. We have found clinically that they save time, cut down on blood loss, and give really adequate closures throughout the entire postoperative period.

It is true that there is variation in the literature. There have been 40 or 50 reports that looked at different techniques of suture and staple closure. I know there are surgeons who have done very well using 3-0 silk and other sutures for closing the bronchus. Superior results have been achieved using both stapled and sutured closures. So, in answer to the first point, Dr Bender is quite correct in saying that it depends on the technique the surgeon uses in closing the tissue. This is especially true with stapling devices because the instrument must be applied in such a way that the tissue is not crushed, which causes late necrosis.

It is also true that the pressures were much in excess of the ones we see physiologically. Basically what we were testing was the tensile strength of these tissues because we could not find that information in the literature. We did stress them to their maximum because we wanted to know what kind of pressures would be tolerated. The best information I could find for maximal pressures was a 1957 article [17] by a group from Brazil who looked at maximum pressures that could be generated in the chest during coughing in healthy young men. They were able to generate pressures up to 200 mm Hg. For this reason we wanted to know what maximal pressures would be required to disrupt closures in the first postoperative day. Obviously the pressures we recorded in the cadaver specimens were comparable with those generated in healthy, coughing young men.

Finally, we think that staples are as good as, indeed better than, sutures for closing the pulmonary artery, pulmonary vein, and large bronchi.

International Society for Heart Research

Kobe City, Japan, May 10–14, 1992

The Richard J. Bing Award for Young Investigators

The International Society for Heart Research invites submissions for the Richard J. Bing Award for Young Investigators. Details of the competition are as follows:

1. Candidates must be members of the International Society for Heart Research (Membership application details are available from Professor D. J. Hearse, Secretary General, ISHR, Cardiovascular Research, Rayne Institute, St. Thomas' Hospital, London SE1 7EH, Great Britain).
2. Submissions must take the form of a manuscript, prepared according to the instructions to authors, for the *Journal of Molecular and Cellular Cardiology*. Submissions not conforming to these guidelines will not be considered.
3. Only one manuscript per author will be considered. The candidate must be the sole or the first author.
4. Ten copies of each manuscript together with 10 copies of the applicant's curriculum vitae should be received by Professor D. J. Hearse, Secretary General of the ISHR, Cardiovascular Research, Rayne Institute, St. Thomas' Hospital, London SE1 7EH, Great Britain, **no later than September 30, 1991.**
5. The manuscript should relate to previously unpublished work and must be accompanied by certification from the candidate's Head of Department that the work was conceived and executed by the candidate, has not been published, and is not currently under consideration for publication elsewhere.
6. Candidates must be less than 36 years of age by May 14, 1992.
7. All submitted works will be evaluated by a committee of the ISHR from which four finalists will be selected. Each finalist will qualify for a travel award of up to US $1,500 toward his/her attendance at the XIVth Annual meeting of the International Society for Heart Research (Kobe, Japan, May 10–14, 1992). All finalists will receive free registration and accommodation for the duration of the meeting.
8. At the meeting, each finalist will verbally present his/her study to the Society. The winner of the Award will receive an award of US $1,500.
9. The prize-winning work will be considered for priority publication (subject to usual refereeing process) in the *Journal of Molecular and Cellular Cardiology*.
10. Submitted manuscripts will not be returned unless specifically requested.

D. J. Hearse
Secretary General

Primary Cardiac Sarcomas

Joe B. Putnam, Jr, MD, Michael S. Sweeney, MD, Rolando Colon, MD, Louis A. Lanza, MD, O. H. Frazier, MD, and Denton A. Cooley, MD

Department of Thoracic Surgery, The University of Texas M.D. Anderson Cancer Center, and Division of Cardiovascular Surgery, Texas Heart Institute, St. Luke's Episcopal Hospital, Houston, Texas

In marked contrast to benign cardiac tumors, primary cardiac sarcomas occur infrequently. Moreover, there is no uniform approach to treating such patients, and the benefits of postoperative chemotherapy are unclear. Between 1964 and 1989, 21 patients with primary cardiac sarcomas underwent surgical resection alone (n = 7), chemotherapy alone (n = 1), or combined operation and postoperative chemotherapy based on adriamycin (n = 13). Twenty-four operations were performed on 20 patients with relief of symptoms in all. Eleven patients had complete resection. Operative mortality was 8.3% (2/24). Histology and originating chamber(s) included angiosarcoma (n = 7; 6/7 in right atrium, 1 in left atrium), malignant fibrous histiocytoma (7; all in left atrium), fibrosarcoma (2; 2/2 in left atrium), rhabdomyosarcoma (2; 1 in left atrium, 1 in right ventricle), leiomyosarcoma (2; 1 in left atrium, 1 in left ventricle); and one undifferentiated sarcoma (right atrium). Overall actuarial survival was 14% at 24 months after resection. Patients with complete resection had a median survival of 24 months compared with only 10 months in all other patients (*p* = 0.035). Postoperative chemotherapy did not enhance survival in patients with incomplete resection. At this time, aggressive and complete surgical resection seems to offer the best hope for palliation and survival in an otherwise fatal disease.

(*Ann Thorac Surg 1991;51:906–10*)

Primary cardiac sarcomas occur rarely, and surgical resection is most often needed to relieve symptoms. In striking contrast to metastatic neoplasms to the heart or pericardium, primary cardiac sarcomas represent a locally aggressive tumor growing into one or more cardiac chambers. These tumors display no symptoms early in their course; only when the tumor obstructs cardiac output will symptoms occur (dyspnea, chest pain, congestive heart failure). Evaluation often reveals a large cardiac tumor or metastases. It is precisely at this stage, with the tumor large and bulky, that patients undergo an attempt at resection. Often the tumor is unresectable because of extensive invasion of myocardium, but with complete resection, symptoms can be attenuated and survival after operation may be improved.

In collected autopsy series, primary tumors of the heart occur with an incidence of 0.001% to 0.28% [1]. Among these primary cardiac tumors in adults, approximately 25% are malignant, most of these being sarcomas [2]. In children, malignant cardiac tumors make up less than 10% of cardiac tumors [3].

Primary cardiac sarcomas usually produce clinical symptoms and require resection to relieve these symptoms [4, 5]. But, because of the limited experience in their treatment, general strategies for management of these sarcomas are less clear. Chemotherapy and radiation therapy do not relieve symptoms as well as operation [4]. In this study we reviewed the initial symptoms, treatment, and outcome of patients with primary cardiac sarcomas treated at our institutions to evaluate outcome and to suggest improved methods of care.

Material and Methods

Between 1964 and 1989, we identified 21 patients from the University of Texas M.D. Anderson Cancer Center and the Texas Heart Institute with primary malignant sarcomas of the heart. Twenty-four operations were performed on these patients (Table 1). There were 11 male and 10 female patients. Their ages ranged from 3 months to 64 years. Two patients were lost to follow-up after operation and excluded from further survival analysis.

The extent of the cardiac tumor was measured by two-dimensional echocardiography and cardiac catheterization in all patients. The surgeon also assessed the extent of tumor intraoperatively for further resection. The presence or absence of metastases was generally assessed by computed tomography.

All patients were symptomatic when first seen. Symptoms included dyspnea (13/21; 61.9%), chest pain (6/21; 28%), congestive heart failure (6/21; 28%), palpitations (5/21; 24%), fever (3/21; 14%), and myalgia (2/21; 10%).

Twenty patients (20/21 patients) underwent 24 operations for resection. One patient (1/21) was not explored owing to extensive extracardiac disease and received chemotherapy only. Only 11 patients (11/20; 55%) had complete resection. The other patients had incomplete resection (8/9; 89%) or biopsy (1/9; 11%). Four patients underwent repeat resection for recurrent tumor. The operative mortality was 8.3% (2/24). We examined patient characteristics, initial symptoms, chamber of origin, ade-

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Presented at the Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association, Dorado, Puerto Rico, Nov 8–10, 1990.

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Table 1. Patient Population With Primary Cardiac Sarcomas

Patient No.	Age (y)	Sex	Histology	Chamber	Resectable	Postop Chemotherapy	Survival (mo)	Status
1	42	M	Angio	RA + RV	No	. . .[a]	. . .[a]	. . .[a]
2	59	M	Angio	RA + RV	No	Yes	10	D
3	27	M	Angio	RA + RV	No	Yes[b]	6	D
4	27	M	Angio	RA + RV	. . .[c]	No[c]	12	D
5	64	M	Angio	RA	Yes	No	0	D[d]
6	58	F	Angio	RA	Yes	No	6	D
7	57	F	Angio	LA	Yes[e]	Yes	15	D
8	40	F	MFH	LA	Yes[e]	Yes	30	D
9	50	F	MFH	LA	Yes	Yes	11	D
10	55	F	MFH	LA	Yes	Yes	24	D
11	40	F	MFH	LA	Yes	Yes	12	D
12	24	M	MFH	LA	No[e]	Yes	24	D
13	35	M	MFH	LA	No	Yes	11	D
14	26	M	MFH	LA + LV	No	. . .[a]	. . .[a]	. . .[a]
15	14	M	Rhabdo	LA	No[f]	Yes	6	D
16	3 mo	F	Rhabdo	RV	Yes	No	54	A, NED
17	38	M	Leiomyo	LV	No	Yes	9	D
18	20	M	Leiomyo	LA	No	No[g]	8	D
19	10	M	Undiff	RA	Yes	Yes	15	A, WD
20	43	F	Fibromyxo	LA	Yes	No[g]	2	D
21	28	F	Myxo	LA	Yes[h]	No	24	D[d]

[a] Lost to follow-up; presumed dead. [b] Radiation therapy also given as adjuvant therapy. [c] No operation; received chemotherapy only. [d] Died <30 days after operation of pump failure. [e] Patient had two resections. [f] Incomplete resection; microscopic positive margins only. [g] Adjuvant therapy not known to have been given. [h] Patient had three resections.

A = Alive; Angio = angiosarcoma; D = dead; Fibromyxo = fibromyxosarcoma; LA = left atrium; Leiomyo = leiomyosarcoma; LV = left ventricle; MFH = malignant fibrous histiocytoma; Myxo = myxosarcoma; NED = no evidence of disease; RA = right atrium; Rhabdo = rhabdomyosarcoma; RV = right ventricle; Undiff = undifferentiated sarcoma; WD = with disease.

quacy of surgical resection, histology, adjuvant treatment, and survival.

Survival curves were calculated using the method of Kaplan and Meier [6]. Comparisons between groups were made using the generalized Wilcoxon test of Gehan [7]. All p values resulted from two-sided tests.

Results

Actuarial Survival

The overall actuarial survival for all patients with primary cardiac sarcomas was 14% at 24 months. The median survival was 11 months (Fig 1).

Symptoms

Symptoms of dyspnea, chest pain, congestive heart failure, palpitations, fevers, and myalgia occurred in all patients. All patients who underwent an attempt at complete resection had improvement in their functional status and attenuation of symptoms.

Resectability

Patients with resectable disease (11/20; 55%) had a better postthoracotomy survival (median survival, 24 months) than patients with unresectable disease (9/20; 45%; median survival, 11 months; $p = 0.035$) (Fig 2).

Histology

All patients had histological confirmation of primary sarcoma of the heart. Seven patients had a histological diagnosis of angiosarcoma (7/21; 33%), 7 patients had

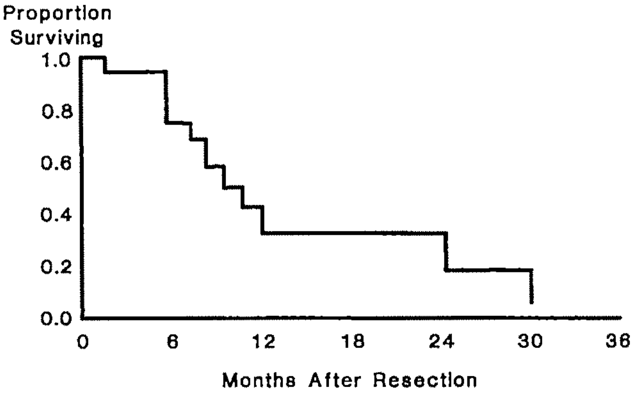

Fig 1. Overall actuarial survival in patients with primary cardiac sarcomas.

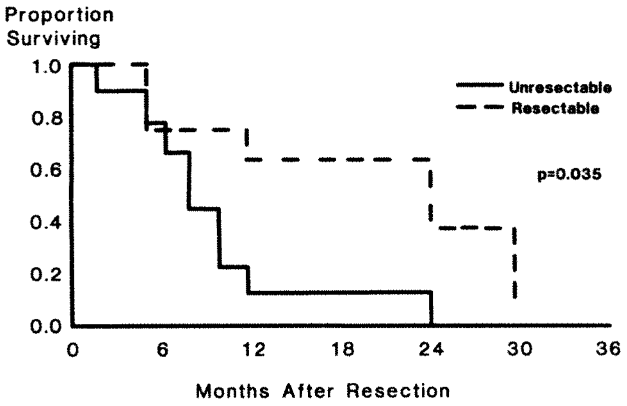

Fig 2. Survival in patients with resectable and unresectable primary cardiac sarcomas.

malignant fibrous histiocytoma (7/21; 33%), 2 patients had rhabdomyosarcoma (2/21; 9.5%), 2 patients had leiomyosarcoma (2/21, 9.5%); and 1 patient each had undifferentiated sarcoma, fibromyxosarcoma, and myxosarcoma. Survival after resection was similar in patients with a histological diagnosis of angiosarcoma and malignant fibrous histiocytoma.

Chamber of Origin

Chamber of origin and age when first seen varied between the different histologies (see Table 1). The mean age of the 7 patients with angiosarcoma was 48.5 years, and six of the seven tumors originated from the right side of the heart (2 right atrium, 4 right atrium and right ventricle). In contrast, all 7 patients with malignant fibrous histiocytoma had tumors that originated from the left side of the heart (6 left atrium, 1 left atrium and left ventricle). The mean age of this group was 38.6 years.

Adjuvant Therapy

Thirteen patients received postoperative adjuvant chemotherapy based on adriamycin, and 1 patient with unresectable disease received chemotherapy alone. The use of postoperative chemotherapy did not appear to improve survival. There was no significant difference in survival in patients who underwent operation alone compared with those patients who had adjuvant chemotherapy after operation.

Cause of Death

The cause of death for most patients was progressive enlargement of the tumor and obstruction of cardiac flow or progressive and unresectable metastases.

Comment

Primary cardiac sarcomas encompass the bulk of primary malignant neoplasms of the heart. The low incidence of primary cardiac sarcomas reflects the overall low incidence of sarcomas in the general population and the small percentage of body weight of the heart (0.5%) compared with muscle (40%) in the individual [8]. Primary cardiac sarcomas account for 20% of all cardiac neoplasms [2]. Patients who have potentially resectable disease are fewer still [2, 4].

Most reported series infrequently describe patients with primary cardiac sarcomas. Reports of response to treatment and survival are anecdotal. Murphy and associates [4] described 12 patients with primary cardiac sarcomas out of 114 patients with primary tumors of the heart. Survival was poor (9 months), but palliation was good. Most patients died of metastatic disease. Other series report similar dismal survival [9–11].

Often tumors are so large at the time of operation that complete resection cannot be done. In one series, 4 of 8 patients with primary malignant cardiac sarcomas did not have complete resection. Three patients (3/8) died within 30 days of operation. Local recurrence or metastases developed in all remaining patients, and all but 1 died within 10 months [12].

Initial Symptoms

Primary cardiac sarcomas can occur at any age with symptoms mimicking other more common cardiopulmonary diseases, usually valvar heart disease [12]. In our patients, obstructive symptoms such as dyspnea, chest pain, and congestive heart failure and constitutional symptoms such as fevers and myalgia commonly occurred.

Evaluation

Our patients had an initial evaluation with two-dimensional echocardiography or angiography [2, 9, 12–14]. Magnetic resonance imaging may be of value in determining the extent of a cardiac neoplasm to better plan resection of the tumor [15]. Despite such techniques, the surgeon often makes the diagnosis of a malignant cardiac tumor in the operating room, and should be ready to do definitive resection then.

Frequent Metastases

Up to 80% of patients with primary cardiac sarcomas may have systemic metastases, particularly to the lungs, when the sarcoma is first diagnosed [2]. Computed tomography of the chest and abdomen can be used when assessing the patient for metastases. Earlier diagnosis may not be possible as symptoms do not occur until the primary tumor is large. Adjuvant therapies may be used, but resolution of symptoms with chemotherapy alone is limited [16, 17].

Surgical Resection

Primary cardiac sarcomas pose a considerable problem to the surgeon because of the late stage at which they are seen and the size of the tumor. In patients with tumor limited to the atrial free wall, the atrial septum, or only a small portion of the ventricle or valve, complete resection should be undertaken. Complete resection is required for improved survival; however, even incomplete resection can provide substantial symptom-free survival in most patients.

All patients in our series had surgical resection attempted except 1 who had advanced extracardiac disease.

Cardiopulmonary bypass was commonly used. All patients who underwent surgical resection, complete or incomplete, had improvement in symptoms. Patients who had complete resection had improved postresection survival compared with patients who had incomplete resection. Although surgical resection results in only few long-term survivors, the improvement in quality of life and potential for longer survival justifies an attempt at surgical resection in these patients with limited life expectancy [8].

Histology and Location Within the Heart

Angiosarcoma (n = 7) and malignant fibrous histiocytoma (n = 7) occurred most frequently. Angiosarcoma may represent the most commonly occurring primary malignant cardiac tumor [1, 5]. In our patients, angiosarcomas arose from the right atrium and ventricle, whereas malignant fibrous histiocytomas arose from the left atrium and ventricle. There was no difference in survival between these two sarcomas. One patient with angiosarcoma died of spontaneous rupture of a liver metastasis with free intraperitoneal bleeding. The findings of right-sided heart failure, chest pain, bloody pericardial effusion, and a mass in the right atrium suggest an angiosarcoma [10, 18].

Malignant fibrous histiocytomas occurred with a frequency equal to that of angiosarcoma in our series, and most of these patients had a presumptive diagnosis of left atrial myxoma. Other tumors seen clinically as left atrial myxomas were fibrosarcoma and myxosarcoma [19].

Rhabdomyosarcoma occurred only in 2 children, in contrast to McAllister's [1] study, where the incidence of rhabdomyosarcoma was second only to angiosarcoma in adults. Even in children, we recommend aggressive surgical resection in all symptomatic patients without metastases [3]. Occult metastases also must be excluded [14].

Adjuvant Therapy

Thirteen patients had postoperative adjuvant therapy (adriamycin based), and 1 patient received chemotherapy alone. Although adriamycin-based chemotherapy effectively treats soft tissue sarcomas in other locations, little evidence supports its efficacy to palliate symptoms in patients with primary cardiac sarcomas. The use of postoperative chemotherapy did not appear to prolong survival in our patients, although it is difficult to evaluate the efficacy of the agents with small numbers of patients [16, 20].

Occasional patients have received radiation therapy for treatment of primary malignant cardiac sarcomas with little effect [8, 11, 21].

Transplantation

Orthotopic cardiac transplantation may represent the treatment of choice for patients with unresectable but locally aggressive tumors involving only the heart. Aravot and associates [22] described a patient who underwent orthotopic cardiac transplantation for a neurofibrosarcoma of the heart and remained well 5.5 years after transplantation without evidence for recurrence. One other patient died while waiting for a donor heart. Aravot and associates suggested that early cardiac transplantation may offer the best hope for these patients. Jamieson and co-workers [23] described a 17-year-old girl with an unresectable left ventricular fibroma and progressive ventricular arrhythmias. She had cardiac transplantation 2 years after the initial diagnosis and had done well for more than 18 months at the time of the report. Gabelman and associates [24] also reported a young woman with multiple local recurrences of a malignant fibrous histiocytoma arising from the left atrial wall. Despite multiple surgical procedures, the tumor recurred locally and the patient died of obstruction of the left atrium. No metastases were identified. Heart-lung transplantation in this patient may have provided substantial palliation and long-term survival.

Summary

Today, patients with primary cardiac sarcomas have a poor prognosis despite treatment. Selection of patients for operation remains difficult as one cannot predict the resectability of these large tumors before operation. We recommend early surgical exploration and resection as the initial treatment of primary cardiac sarcomas. Completeness of resection will depend on location of the tumor, extent of invasion in the myocardium and cardiac skeleton, and histology. Patients with primary cardiac sarcomas without metastases should undergo exploration and resection for: (1) local control of the primary tumor, (2) relief of obstructive symptoms, and (3) potential for longer survival with effective adjuvant therapy. Though operative mortality and morbidity may be high, complete resection will yield twice the long-term survival as that of unresectable patients with significant symptom-free survival.

References

1. McAllister HA. Primary tumors of the heart and pericardium. Curr Probl Cardiol 1979;4:1–51.
2. Silverman NA. Primary cardiac tumors. Ann Surg 1980;191:127–38.
3. Arciniegas E, Hakimi M, Farooki ZQ, Truccone NJ, Green EW. Primary cardiac tumors in children. J Thorac Cardiovasc Surg 1980;79:582–91.
4. Murphy MC, Sweeney MS, Putnam JB Jr, et al. Surgical treatment of cardiac tumors: a 25-year experience. Ann Thorac Surg 1990;49:612–7.
5. Chitwood WR Jr. Cardiac neoplasms: current diagnosis, pathology and therapy. J Cardiac Surg 1988;3:119–54.
6. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–81.
7. Gehan EA. A generalized Wilcoxon test for comparing arbitrarily singly-censored samples. Biometrika 1965;52:203–23.
8. Sanoudos G, Reed GE. Primary cardiac sarcoma. J Thorac Cardiovasc Surg 1972;63:482–5.
9. Bear PA, Moodie DS. Malignant primary cardiac tumors. The Cleveland Clinic experience, 1956 to 1986. Chest 1987;92:860–2.
10. Reece IJ, Cooley DA, Frazier OH, Hallman GL, Powers PL, Montero CG. Cardiac tumors. Clinical spectrum and prognosis of lesions other than classical benign myxoma in 20 patients. J Thorac Cardiovasc Surg 1984;88:439–46.
11. Poole GV Jr, Breyer RH, Holliday RH, et al. Tumors of the

heart: surgical considerations. J Cardiovasc Surg (Torino) 1984;25:5–11.
12. Dein JR, Frist WH, Stinson EB, et al. Primary cardiac neoplasms. Early and late results of surgical treatment in 42 patients. J Thorac Cardiovasc Surg 1987;93:502–11.
13. Klima T, Milam JD, Bossart MI, Cooley DA. Rare primary sarcomas of the heart. Arch Pathol Lab Med 1986;110:1155–9.
14. Chan HS, Sonley MJ, Moes CA, Daneman A, Smith CR, Martin DJ. Primary and secondary tumors of childhood involving the heart, pericardium, and great vessels. A report of 75 cases and review of the literature. Cancer 1985;56:825–36.
15. Watanabe AT, Teitelbaum GP, Henderson RW, Bradley WG Jr. Magnetic resonance imaging of cardiac sarcomas. J Thorac Imaging 1989;4:90–2.
16. Vergnon JM, Vincent M, Perinetti M, Loire R, Cordier JF, Brune J. Chemotherapy of metastatic primary cardiac sarcomas. Am Heart J 1985;110:682–4.
17. Herhusky MJ, Gregg SB, Virmani R, Chun PK, Bender H, Gray GF Jr. Cardiac sarcomas presenting as metastatic disease. Arch Pathol Lab Med 1985;109:943–5.
18. Shackell M, Mitko A, Williams PL, Sutton GC. Angiosarcoma of the heart. Br Heart J 1979;41:498–503.
19. Attum AA, Johnson GS, Masri Z, Girardet R, Lansing AM. Malignant clinical behavior of cardiac myxomas and "myxoid imitators." Ann Thorac Surg 1987;44:217–22.
20. Larrieu AJ, Jamieson WR, Tyers GF, et al. Primary cardiac tumors: experience with 25 cases. J Thorac Cardiovasc Surg 1982;83:339–48.
21. Baldelli P, De Angeli D, Dolara A, Diligenti LM, Marchi F, Salvatore L. Primary fibrosarcoma of the heart. Chest 1972;62:234–6.
22. Aravot DJ, Banner NR, Madden B, et al. Primary cardiac tumours—is there a place for cardiac transplantation. Eur J Cardiothorac Surg 1989;3:521–4.
23. Jamieson SW, Gaudiani VA, Reitz BA, Oyer PE, Stinson EB, Shumway NE. Operative treatment of an unresectable tumor of the left ventricle. J Thorac Cardiovasc Surg 1981;81:797–9.
24. Gabelman C, Al Sadir J, Lamberti J, et al. Surgical treatment of recurrent primary malignant tumor of the left atrium. J Thorac Cardiovasc Surg 1979;77:914–21.

DISCUSSION

DR ROBERT H. JOHNSTON, JR (Houston, TX): I recently had an opportunity to care for a 31-year-old man with acute pericardial tamponade from an angiosarcoma of the right atrium. This was able to be resected; however, there were positive margins at microscopic examination. This man has been treated with chemotherapy for 6 months and is now negative for disease. He is being considered for transplantation. Do you have transplantation in your plan for caring for these patients?

DR COLON: We have not performed cardiac transplantation at the Texas Heart Institute for cardiac sarcoma. However, it has been done, and it should be considered an alternative treatment. Cardiac transplantation should be a matter of timing. If you perform a complete resection, the site of the residual tumor should be considered, because it can become a technical point at the time of orthotopic cardiac transplantation. If you perform a complete resection and the left atrium is uninvolved and you have an adequate cuff of the right atrium or superior and inferior vena cava, transplantation should be a possibility. If donors are available, then the waiting period should be short, and that way the patient may benefit.

DR SAFUH ATTAR (Baltimore, MD): Do you do an extensive search in these patients for metastatic disease before operation? If you do find evidence of a single metastasis, let us say in the brain, would you go ahead with the operation and remove the primary tumor?

DR COLON: As I stated before, most of these patients' diagnoses of sarcoma were arrived at postoperatively or in the operating room. It is very difficult to have a preoperative diagnosis of cardiac sarcoma.

There was a patient in whom metastasis to his mandible developed in the early postoperative course. We cannot do a complete work-up preoperatively because most of the time we do not know we are dealing with this type of lesion.

If a patient has brain metastasis, then it all depends on the extent of that brain metastasis. There are some neurosurgeons who can resect a solitary metastasis to the brain. However, as I stated before, most of these lesions are diagnosed after operation.

DR JOHN D. HARRAH (Huntington, WV): One of the patients you presented may have been one of ours. This patient is a 60-year-old woman in whom we performed resection of 80% to 90% of her right atrium; she had a complete resection. She was referred to M.D. Anderson Cancer Center and was given adriamycin therapy. She survived 2½ years, dying of heart failure caused by adriamycin toxicity. Have you had other cases where the primary tumor was removed with no evidence of recurrence with subsequent demise due to adriamycin toxicity?

DR COLON: We have had patients in whom on postmortem examination the heart has no evidence of recurrent disease; however, they had distant disease, especially in angiosarcomas. One of our patients died of hemoperitoneum after rupture of a hepatic metastasis. We have not reported any from the other group who have died of adriamycin toxicity; however, this was a limited group of patients.

Reducing Postischemic Paraplegia Using Conjugated Superoxide Dismutase

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Paraplegia after thoracic aortic aneurysm repair has an incidence of 2.2% to 24%. Oxygen-derived free radicals after reperfusion of an ischemic spinal cord may be partly responsible for neuronal destruction. We studied the effects of polyethylene glycol–conjugated superoxide dismutase (PEG-SOD), a free radical scavenger, as a way of increasing spinal cord tolerance to ischemia. Thirty rabbits underwent 40 minutes of aortic occlusion (a known model of paraplegia). Ten of these animals received 25,000 U/kg of PEG-SOD 24 hours before aortic occlusion and two additional doses of 10,000 U/kg, one before and one subsequent to spinal ischemia. Ten animals received superoxide dismutase in the same dosages as those receiving PEG-SOD. Ten control animals received placebo. All animals were studied for 96 hours, at which time a final neurological examination was performed and the results were recorded. Of the 10 animals treated with PEG-SOD, 2 were completely paralyzed whereas 8 had less (7) or no (1) neurological impairment. Eight of the 10 control animals and 9 of the 10 animals receiving superoxide dismutase were completely paralyzed. None of the control animals or animals receiving superoxide dismutase had a normal neurological examination ($p \leq 0.05$). Treatment with PEG-SOD before and during occlusion increased the rabbit spinal cord tolerance to a 40-minute ischemic insult. Scavenging free radicals may lessen experimental spinal cord injury.

(Ann Thorac Surg 1991;51:911–5)

Repair of aneurysms of the descending thoracic aorta is associated with paraplegia with an incidence ranging from 2.2% to 24% [1]. Factors contributing to spinal cord ischemia include the time of aortic occlusion, systemic hypotension, loss of spinal cord blood supply, postischemic hyperemia resulting in spinal cord edema, a decrease in spinal cord perfusion pressure, and reperfusion injury that may be due to oxygen-derived free radicals [2–4]. Cardiopulmonary bypass, heparin-coated vascular shunts, and left atrial bypass have been used to improve blood flow to the body below the aortic clamp, but this improvement in blood flow has not resulted in a decreased incidence of paraplegia [5]. McCullough and associates [6] demonstrated that drainage of cerebrospinal fluid could increase spinal cord perfusion pressure and decrease the incidence of paraplegia in a canine model.

Besides the primary ischemic injury, an additional injury to the spinal cord may occur during the reperfusion period. Oxygen-derived free radicals are known to be produced in ischemic tissues and represent a potential mechanism for tissue injury and vascular dysfunction [7]. Oxygen-derived free radical scavengers such as superoxide dismutase and catalase have been shown to be important enzymes in the control of free radicals. Superoxide dismutase is limited in its effectiveness because of its half-life of 6 minutes and because of its inability to pass readily through the cell membranes of the central nervous system [8]. Superoxide dismutase has been conjugated to polyethylene glycol (PEG-SOD), which increases the circulatory half-life of this enzyme from 6 minutes to 38 hours and appears to facilitate its intracellular access [9]. Thus, this conjugated form of superoxide dismutase provides a more effective means of scavenging free radicals.

Material and Methods

Perioperative Care and Assessment

Thirty New Zealand albino male rabbits, weighing 3.0 to 4.0 kg each (mean weight, 3.8 kg), were anesthetized with intramuscular ketamine (10 mg/kg). No animal received ventilatory or blood pressure support. The animals were then placed in a halothane hood with a mixture of 1.0% to 1.5% halothane for maintenance of anesthesia and administration of supplemental oxygen (Fig 1). A rectal probe and a warming pad were used to regulate core temperature.

After sterile surgical preparation, a 5-cm midline abdominal incision was performed. The abdominal aorta was then mobilized for a length of 1 cm immediately beneath the left renal artery. Bilateral groin incisions allowed mobilization and control of both femoral arteries. A long 4F Silastic (Dow Corning Corp, Midland, MI) catheter was advanced through one femoral artery to a location 1 to 1.5 cm just above the left renal artery. The positioning of this catheter was confirmed by direct vision and palpation through the abdominal incision. An additional 4F Silastic catheter was placed into the opposite

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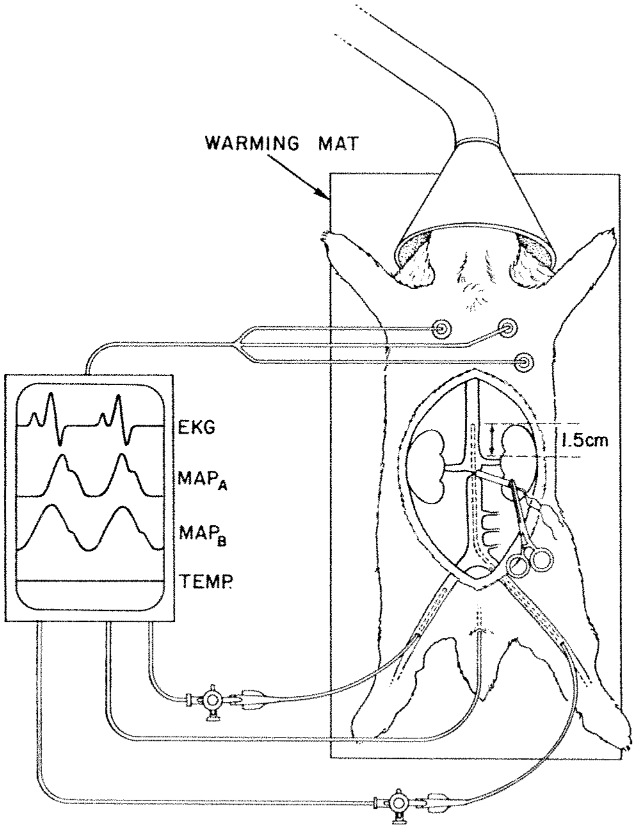

Fig 1. The rabbit model used to create spinal cord ischemia. (EKG = *electrocardiogram;* MAP = *mean arterial pressure.)*

femoral artery and advanced to a point just proximal to the inguinal ligament. These catheters were attached to transducers (model 1290C; Hewlett Packard, Andover, MA) and used to monitor proximal systemic blood pressure as well as distal abdominal aortic blood pressure.

Occlusion of the rabbit abdominal aorta immediately below the left renal artery produces spinal cord ischemia because the rabbit has segmental arteries supplying the spinal cord below the left renal artery without any major collateral arteries to the lumbosacral cord originating above the left renal artery. Each rabbit received 150 U/kg of heparin before aortic occlusion and 3.0 mg of protamine sulfate at the conclusion of the procedure. Preoperatively, cefonicid (Monocid; Smith Kline & French Laboratories, Philadelphia, PA) was injected intravenously over 5 minutes at a dose of 10 mg/kg. The infrarenal aorta was not occluded until the rabbit's arterial pressures equilibrated to near-normal values for at least 10 minutes. Occlusion was obtained by securing a Rumel arterial occluder just below the left renal artery and observing the distal occlusive arterial pressure until it approached the venous pressures. The infrarenal aorta was occluded for 40 minutes in all experimental animals. The arterial catheters were removed at the end of the procedure, the superficial femoral arteries were ligated, and all incisions were closed. Postoperatively fluids were given by intraperitoneal injection.

The animals were observed for 96 hours, at which time their final neurological examination was performed and the animals were killed by ketamine and halothane overdose. The animals were neurologically graded according to the following scale: normal (normal hop), weak (paretic, spastic hind limbs, variable bladder and bowel function), and paralyzed (flaccid paraplegia without bowel or bladder control).

The 30 rabbits were divided into three groups of 10 each: a control group, a superoxide dismutase group, and a PEG-SOD group. Each animal was treated the same except for the injection of the study agents or the injection of normal saline solution in the control animals.

One study group received 25,000 U/kg of PEG-SOD (Sterling Drug, Inc, Rensselaer, NY) 24 hours before the ischemic procedure by intravenous injection through an ear vein over 5 minutes. Just before spinal cord ischemia, these rabbits received 10,000 U/kg of PEG-SOD through the suprarenal Silastic catheter, and another 10,000 U/kg of this material was given through the same catheter during the reperfusion phase after the catheter had been pulled back to a location just within the femoral artery. This catheter was pulled back to ensure optimal aortic blood flow. The second study group received unconjugated superoxide dismutase at the same dosage, schedule, and route as those receiving PEG-SOD. The control animals underwent injections of normal saline solution of equal volumes and at similar times to those animals receiving conjugated and unconjugated superoxide dismutase. No attempt was made to measure levels of PEG-SOD in cerebrospinal fluid or spinal cord tissue.

This research protocol was reviewed and approved by the Animal Research Committee at the University of Virginia Medical Center. The care for these animals complied with the "Principles of Laboratory Animal Care" and the "Guide for the Care and the Use of Laboratory Animals" (National Institutes of Health publication No. 85-23, revised 1985).

Statistical Analysis

All values are expressed as mean ± standard error of the mean. Comparisons among experimental groups were performed using two-way analysis of variance. Frequency data were compared using a χ^2 analysis. Significance was considered achieved when p was less than 0.05. All analyses were performed using the PC version of the Statistical Analysis System run on a Dell System 200.

Results

There was some fluctuation in the neurological examination results during the 96 hours after occlusion. At 24 hours after aortic occlusion, there were 3 (30%) PEG-SOD animals, 10 (100%) SOD animals, and 9 (90%) control animals that were paralyzed. Over the next 24 hours spastic hind limbs developed in 1 paralyzed animal from the control group, which was then considered no longer completely paralyzed and was classified as weak. Likewise, 1 PEG-SOD animal and 1 SOD animal that initially appeared paralyzed became paretic. In the PEG-SOD group, there were 2 (20%) animals considered normal at 24 hours, but during the next 48 hours one of these

Table 1. Neurological Status at 96 Hours[a]

Neurological Status	PEG-SOD	SOD	Control
Normal	1	0	0
Weak	7	1	2
Paralyzed	2	9	8

[a] $p < 0.05$ for paralysis in PEG-SOD versus SOD or control animals.

PEG = polyethylene glycol; SOD = superoxide dismutase.

animals demonstrated mild right hind limb weakness, and this persisted until termination of the study without signs of improvement.

The neurological status of all rabbits at 96 hours is depicted in Table 1. At no time were any of the control or unconjugated SOD animals considered to be normal. Only 2 (20%) of the animals that received PEG-SOD were paralyzed compared with 8 (80%) of the control animals and 9 (90%) of the SOD-treated animals ($p < 0.05$).

There were no significant differences in hemodynamic variables between those animals that received PEG-SOD and those that did not (Table 2). Also, no significant hemodynamic differences were noted between those animals in which complete paraplegia developed and those that were not completely paralyzed (Table 3). There were no significant differences between the PEG-SOD, SOD, and control animals or between the paralyzed and nonparalyzed rabbits in temperature, blood pressure, aortic occlusion time, or other cardiovascular variables.

Comment

Spinal cord injury after thoracic aortic cross-clamping is a persistent clinical problem, occurring in about 5% to 10% of cases. There seem to be three phases of injury: the initial ischemic injury, a reduction in blood flow after a hyperemic phase which may be a compartment syndrome, and an injury that seems to be mediated by free radicals. Clinically, and in the laboratory, preventive efforts are directed primarily to decreasing direct spinal cord ischemia. All surgeons strive for the minimum aortic occlusion time [10,11]. Many surgeons suggest that reimplantation of intercostal arteries should be done when feasible, although conclusive data supporting this practice are lacking [12]. Other intraoperative factors considered important include avoiding systemic hypotension [2], increasing spinal cord perfusion pressures with various shunts and bypass techniques [13], and decreasing the metabolic demands of spinal cord tissue [14].

There is evidence that postischemic hyperemia is associated with paraplegia after aortic cross-clamping [3]. Drainage of cerebrospinal fluid has been shown to reduce spinal cord injury after ischemia in an animal model [6]. These findings have led to speculation that part of the postischemic spinal cord injury may be caused by a late reduction in blood flow secondary to a compartment syndrome. There is increasing evidence that free radicals result from ischemia and contribute to postischemic injury [15]. Although superoxide dismutase has been administered in an attempt to scavenge these free radicals, its effectiveness has been questioned [16]. Other free radical scavengers have been used in this clinical situation including steroids [17] and dimethyl sulfoxide [18]. However, none of these scavengers seems to be practical for clinical use [16]. Polyethylene glycol as a carrier has been used clinically and is believed to have an acceptable safety profile for use in humans [19].

A recent study showed that superoxide dismutase conjugated to polyethylene glycol can reduce ischemic brain injury in experimental animals [20]. This conjugation increases the half-life of superoxide dismutase from less than 10 minutes to 38 hours [9]. These reports prompted our study to examine the usefulness of the conjugated superoxide dismutase in reducing spinal cord injury after ischemia. Our results show that conjugated superoxide dismutase reduces the severity of neurological injury in this model. Only 20% of the animals that received the conjugated superoxide dismutase were paralyzed compared with 90% of the animals receiving unconjugated superoxide dismutase and 80% of the control animals ($p < 0.05$). Reduction in paralysis in clinical practice might similarly be influenced by the administration of this type of conjugated free radical scavenger.

In summary, there seems to be an element of postischemic spinal cord injury mediated by free radicals. Our evidence supports this concept. Our data also show that superoxide dismutase conjugated with polyethylene glycol, with its prolonged half-life, is significantly better at preventing paralysis than is the unconjugated form of superoxide dismutase. Use of this compound may be

Table 2. Hemodynamic Variables by Group[a]

	Baseline			Occlusion			Reperfusion		
Variable	PEG-SOD	SOD	Control	PEG-SOD	SOD	Control	PEG-SOD	SOD	Control
Heart rate (bpm)	201 ± 13	205 ± 11	210 ± 10	215 ± 14	221 ± 18	220 ± 16	230 ± 20	210 ± 17	215 ± 18
Mean proximal arterial pressure (mm Hg)	65 ± 8	68 ± 12	62 ± 15	69 ± 13	69 ± 17	66 ± 13	NA[b]	NA[b]	NA[b]
Mean distal pressure arterial (mm Hg)	53 ± 5	49 ± 7	50 ± 8	15 ± 6	14 ± 6	15 ± 4	55 ± 8	56 ± 11	58 ± 9
Temperature (°C)	35 ± 2	35 ± 3	35 ± 1	33 ± 1	33 ± 4	34 ± 3	33 ± 2	34 ± 1	33 ± 3

[a] p = not significant for all values. [b] The proximal catheter was pulled back during reperfusion.

NA = not available; PEG = polyethylene glycol; SOD = superoxide dismutase.

Table 3. Hemodynamic Variables for Paralyzed Versus Nonparalyzed Animals[a]

Variable	Baseline		Occlusion		Reperfusion	
	Nonpara	Para	Nonpara	Para	Nonpara	Para
Heart rate (bpm)	211 ± 15	218 ± 13	208 ± 9	218 ± 6	209 ± 7	221 ± 12
Mean arterial pressure proximal (mm Hg)	64 ± 9	62 ± 12	72 ± 11	67 ± 9	NA[b]	NA[b]
Mean arterial pressure distal (mm Hg)	51 ± 8	56 ± 11	15 ± 6	16 ± 5	58 ± 8	52 ± 13
Temperature (°C)	35 ± 1	35 ± 1	33 ± 2	33 ± 1	34 ± 3	33 ± 2

[a] p = not significant for all values. [b] The catheter was pulled back during reperfusion so proximal pressures were not measured at that time.

NA = not available; Nonpara = nonparalyzed; Para = paralyzed.

clinically applicable when thoracic aortic cross-clamping is required.

References

1. Livesay JJ, Cooley DA, Ventemiglia RA, et al. Surgical experience in descending thoracic aneurysmectomy with and without adjuncts to avoid ischemia. Ann Thorac Surg 1985; 39:37–46.
2. Crawford ES, Rubino P. Reappraisal of adjuncts to avoid ischemia in the treatment of aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1973;66:693–702.
3. Barone GW, Joob AW, Flanagan TL, Dunn CE, Kron IL. The effect of hyperemia on spinal cord function after temporary thoracic aortic occlusion. J Vasc Surg 1988;8:535–40.
4. Lim KH, Connolly M, Rose D, et al. Prevention of reperfusion injury of the ischemic spinal cord: use of recombinant superoxide dismutase. Ann Thorac Surg 1986;42:282–6.
5. Robertson CS, Foltz R, Grossman RG, Goodman JC. Protection against experimental ischemic spinal cord injury. J Neurosurg 1986;64:633–42.
6. McCullough JL, Hollier LH, Nugent M. Paraplegia after thoracic aortic occlusion: influence of cerebrospinal fluid drainage. J Vasc Surg 1988;7:153–60.
7. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 1985;312:159–63.
8. Turrens JF, Crapo JD, Freeman BA. Protection against oxygen toxicity by intravenous injection of liposome-entrapped catalase and superoxide dismutase. J Clin Invest 1984;73: 87–95.
9. Beckman JS, Minor RL Jr, White CW, Repine JE, Rosen GM, Freeman BA. Superoxide dismutase and catalase conjugated to polyethylene glycol increases endothelial enzyme activity and oxidant resistance. J Biol Chem 1988;263:6884–92.
10. Najafi H, Javid H, Hunter J, et al. Descending aortic aneurysmectomy without adjuncts to avoid ischemia. Ann Thorac Surg 1980;30:326–35.
11. Crawford ES, Waler HS, Saleh SA, et al. Graft replacement of aneurysm in descending thoracic aorta: results without bypass or shunting. Surgery 1981;89:73–85.
12. DeBakey ME, McCollum CH, Graham JM. Surgical treatment of aneurysms of the descending thoracic aorta: long term results in 500 patients. J Cardiovasc Surg (Torino) 1978;19: 571–6.
13. Laschinger JC, Cunningham JN Jr, Nathan IM, et al. Experimental and clinical assessment of the adequacy of partial bypass in maintenance of spinal cord blood flow during operation on the thoracic aorta. Ann Thorac Surg 1983; 36:417.
14. Coles JG, Wilson GJ, Sima AF, et al. Intra-operative management of thoracic aortic aneurysm: experimental evaluation of perfusion cooling of the spinal cord. J Thorac Cardiovasc Surg 1983;85:292–9.
15. Cuevas P, Carceller-Benito F, Reimers D. Administration of bovine superoxide dismutase prevents sequelae of spinal cord ischemia in the rabbit. Anat Embryol 1989;179:251–5.
16. Kirshner DL, Kirshner RL, Heggeness LM, DeWeese JA. Spinal cord ischemia: an evaluation of pharmacologic agents in minimizing paraplegia after aortic occlusion. J Vasc Surg 1989;9:305–8.
17. Laschinger JC, Cunningham JN, Cooper MM, Krieger K, Nathan IM, Spencer FC. Prevention of ischemic spinal cord injury following aortic cross-clamping: use of corticosteroids. Ann Thorac Surg 1984;38:500–7.
18. Coles JC, Ahmad SN, Mehta HV, Kaumann JC. Role of free radical scavenger in protection of the spinal cord during ischemia. Ann Thorac Surg 1986;41:551–6.
19. Pegademase-adenosine deaminase. Med Lett 1990;32:87–8.
20. Liu TH, Beckman JS, Freeman BA, Hogan EL, Hsu CY. Polyethylene glycol-conjugated superoxide dismutase and catalase reduce ischemic brain injury. Am J Physiol 1989; 256(Heart Circ Physiol 25):H589–93.

DISCUSSION

DR JAMES R. STEWART (Nashville, TN): As you know, we have been interested in this problem for some time, and Dr Gerhardt in our laboratories has performed similar experiments in this model a few years ago.

Confirming what has been mentioned already, there is usually not only a segmental supply but a single blood vessel that supplies the spinal cord in rabbits, and it is very important to occlude the aorta below the renal arteries but above this branch that can be identified going posterior and supplying the spinal cord. We did similar experiments.

Looking at sham-operated animals as well as free radical scavengers, mannitol, pretreatment for 48 hours with allopurinol at a high dose, thiopental, and then various doses and preparations of superoxide dismutase, the only intervention in our studies that provided some protection of the spinal cord was administration of 10 mg/kg of thiopental before aortic occlusion.

As I mentioned, we studied various doses and varieties of superoxide dismutase. High-dose superoxide dismutase really showed no benefit, nor did dimethyl sulfoxide.

Do you have any data comparing PEG-SOD with thiopental?

DR AGEE: We thought about it initially, but there were data such as yours and others that had been published previously that did show a benefit of thiopental. Thus, we decided not to repeat these studies at this time.

DR STEWART: What I was concerned with specifically was that thiopental and superoxide dismutase may have a combined protective effect, so it might be nice to study the combination of PEG-SOD and thiopental.

DR AGEE: We agree that combining these adjuncts may have a cumulative benefit.

DR TIMOTHY J. GARDNER (Baltimore, MD): I think that we can accept your theory of efficacy with PEG-SOD based on its extended half-life. I wonder if you could review the evidence that PEG-SOD is better or has an intracellular penetrance that is superior to that observed with unmodified SOD.

DR AGEE: The data demonstrating cellular penetrance came from one study published by Liu and others in the *American Journal of Physiology* in 1989. Their model involved cold ischemic injury to the brain. This report described significant benefit from the PEG-SOD in recovery of the ischemic insult to brain tissue. The study did not quantitate the ability of the PEG-SOD to penetrate the intracellular compartment, nor do we have other such data available.

DR GARDNER: The problem with the hypothermia studies is that you may have altered cell membrane function. I am skeptical that PEG-SOD has better intracellular penetrance than superoxide dismutase that is not conjugated.

DR AGEE: We would agree. Thank you for your comments.

DR WILLIAM A. BAUMGARTNER (Baltimore, MD): Did you in your studies make any indirect measurements that free radicals are even generated during your period of ischemia? There are some studies such as conjugated dienes and other biochemical studies with which you can indirectly measure generation of free radicals, which might provide more evidence that indeed the combination of polyethylene glycol with superoxide dismutase does provide more efficacy over controls.

DR AGEE: No, we did not measure the production of free radicals in our model.

DR RICHARD E. CLARK (Pittsburgh, PA): Can you tell us what the placebo was that you used?

DR AGEE: The control was normal saline solution.

DR CLARK: You did not have an adequate control, because polyethylene glycol has been used to dissolve many drugs and has a cellular effect on its own. The second control you needed here was a group given the same amount of polyethylene glycol. It does penetrate cells, and it can be shown to have preserving qualities in heart, lung, and brain.

DR AGEE: Yes, the literature reviewed demonstrated exactly what you said. Unfortunately, polyethylene glycol of the proper molecular weight was not available to us at the time of this study.

DR HARVEY I. PASS (Bethesda, MD): Along the same lines, do you actually know how stable your PEG-SOD is? Specifically do you know that it is not deconjugating after you give the substance?

DR AGEE: The data for the stability were provided by the Sterling Drug Company.

Mitral Valve Replacement Combined With Coronary Artery Operation: Determinants of Early and Late Results

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Mitral valve replacement combined with coronary artery bypass grafting has been reported as being associated with a higher mortality than either mitral valve replacement or coronary artery bypass grafting alone. Cause of mitral valve disease and severity of mitral regurgitation have been reported as related to mortality. To study the correlation of the cause of mitral valve disease and severity of mitral regurgitation to hospital mortality and long-term survival, we analyzed the results of 135 patients undergoing mitral valve replacement and coronary artery bypass grafting between June 1974 and August 1989. The hospital mortality was 11.8% (16/135). Fifteen preoperative and operative variables were tested for correlation with hospital or late mortality using univariate tests and multivariate regression. Advanced age (>60 years), New York Heart Association functional class, and wall motion score were independently associated with hospital mortality ($p < 0.05$). The cause of mitral valve disease and severity of mitral regurgitation were not related to hospital mortality or long-term survival ($p > 0.05$). The follow-up rate was 96.6% for the hospital survivors (115/119). Mean follow-up was 52.6 ± 4.1 months. There were 35 late deaths. Survival was 91.9%, 89.9%, 78%, and 49.9% at 1, 2, 5, and 10 postoperative years, respectively. Preoperative New York Heart Association functional class and use of catecholamines during the postoperative intensive care period were independently related to late survival ($p < 0.05$). In conclusion, this study suggested that operative mortality for mitral valve replacement combined with coronary artery bypass grafting was correlated with preoperative New York Heart Association functional class, advanced age (>60 years), and wall motion score, and that long-term survival was correlated with preoperative New York Heart Association functional class and use of catecholamines postoperatively. Neither cause of mitral valve disease nor severity of mitral regurgitation was correlated with hospital or long-term survival.

(Ann Thorac Surg 1991;51:916–23)

The frequency of mitral regurgitation in patients with ischemic heart disease has been estimated between 4% and 31% depending on the severity of the coronary artery disease [1, 2]. Mechanisms for the incompetence include papillary muscle rupture or ischemia. Patients with mitral valve disease due to other causes may also have ischemic heart disease, and if submitted to valve operation may require coronary artery bypass grafting (CABG) as part of the operation. The mortality of the combined operation has been reported as being high [3]. Reported rates of perioperative deaths range from 14% to 24% [4]. The predictors of early and late survival are controversial. In a study by Czer and associates [5], the cause of mitral valve disease was correlated with both early and late survival. However, Lytle and co-workers [4] found that the pathology of the mitral valve disease was not related to in-hospital mortality but related to late survival. Severity of ischemic mitral regurgitation has been demonstrated to be related to late survival [6], but the effects of the severity of mitral regurgitation from other causes on survival are still unclear. In this study, we report our experience with 135 patients who underwent mitral valve replacement (MVR) combined with CABG between June 1974 and August 1989. Particular attention was paid to the correlation between cause of mitral valve disease or severity of mitral valve regurgitation and early or late survival.

Material and Methods

Clinical Material

From June 1, 1974, through August 31, 1989, 135 patients underwent MVR and CABG. Mean age of the patients was 61.48 ± 0.65 years. All operative reports were reviewed to determine the pathology and operative details. Medical charts were also reviewed for preoperative and

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Table 1. Preoperative Data in 135 Patients Undergoing Mitral Valve Replacement and Coronary Artery Bypass Grafting

Variable	No. of Patients	Deaths	Mortality (%)	p Value
Sex				0.25
M	77	7	9.09	
F	58	9	15.52	
Age				0.035
>60 years	86	14	16.28	
<60 years	49	2	4.08	
Angina (CHC)				0.89
No angina	48	7	15.48	
I	5	1	20.0	
II	18	2	11.11	
III	25	2	8.0	
IV	39	4	10.26	
NYHA class				0.032
I/II	2/9	0	0	
III	55	3	5.45	
IV	69	13	18.84	
Atrial fibrillation				0.174
Yes	47	8	17.02	
No	88	8	9.09	
Previous infarction				0.299
Yes	76	11	14.47	
No	59	5	8.47	
Interval between recent infarction and operation				0.295
<24 hours	1	0	0	
2–7 days	2	1	50	
0.5–3 months	19	2	10.53	
>3 months	37	2	5.41	
No infarction	76	11	14.47	
Cardiac enlargement				0.61
Normal	46	6	13.0	
Mild	50	5	10	
Moderate	25	2	8	
Gross	14	3	21.4	

CHC = Canadian Heart class; NYHA = New York Heart Association.

pathological findings. The late survival was assessed as described in a following section.

Preoperative Data

Preoperative data are shown in Table 1. All patients underwent preoperative left heart catheterization and coronary angiography. Patients were grouped into categories of single-, double-, or triple-vessel or left main artery disease. Serious coronary artery disease was defined as 70% or greater stenosis in any view of the right, left anterior descending, or left circumflex artery or their major branches. Left main artery disease was defined as 50% or greater stenosis.

According to left ventriculography, wall motion was scored in 70 patients. The method described in the Coronary Artery Surgery Study was used to determine the score [7–9]. Ventricular function was defined by wall motion score (WMS), with normal being 5, mild being 6 to 10, moderate being 11 to 15, and severe impairment of the left ventricular motion being 16 to 20 [6]. Table 2 lists the catheterization findings. Severity of mitral regurgitation was assessed by left ventriculogram. Mild regurgitation was defined in the right anterior oblique view as left atrial opacification occurring during injection and clearing in one cardiac cycle. Moderate regurgitation was defined as complete filling of the left atrium to the same density as the ventricle, lasting one to two cardiac cycles. Severe regurgitation was defined as complete filling of the left atrium extending into the pulmonary veins, usually lasting more than two cardiac cycles [6].

Criteria of Valve Pathology

One hundred thirty-five patients were divided into four groups based on the Cleveland Clinic's criteria for mitral valve pathology [4]. Pathological changes were described by both surgeons and pathologists. By review of clinical, operative, and histological findings 135 patients were divided into categories of ischemic, rheumatic, degenerative, and infective (bacterial endocarditis) disease. The criteria for categorization were as follows [4]:

Ischemic: Operative findings of a ruptured papillary muscle (6 patients) or operative or histological documentation of a nonruptured but infarcted papillary muscle (6 patients), or previous myocardial infarction and mitral valve insufficiency without clear documentation of papillary muscle necrosis or rupture and without serious rheumatic or degenerative valve pathology (24 patients).

Table 2. Catheterization Data and Hospital Mortality

Variable	No. of Patients	Deaths	Mortality (%)	p Value
No. of vessels stenosed				0.027
One	40	3	7.5	
Two	40	5	12.5	
Three	41	3	7.32	
Left main	14	5	35.71	
Mitral regurgitation				0.64
Nil/mild	68	8	11.76	
Moderate	40	6	15.0	
Severe	27	2	7.41	
Cardiac index (L/m^2)				0.355
>1.5	105	11	10.48	
<1.5	30	5	16.67	
Wall motion score				0.017
5–10	53	3	5.66	
11–15	15	4	26.67	
16–20	2	1	50	

Table 3. Mitral Valve Pathology and Hospital Mortality[a]

Pathology	No. of Patients	Deaths	Mortality (%)
Ischemic	36	4	11.11
Ruptured papillary muscle	6	0	
Infarcted papillary muscle	6	0	
Previous infarction, no myxoid change	24	4	
Rheumatic	48	6	12.5
MS/MS + MI	38	6	
MI	10	0	
Degenerative	48	5	10.42
Bacterial endocarditis	3	1	

[a] No significant difference between groups ($p > 0.05$).
MI = mitral insufficiency; MS = mitral stenosis.

Rheumatic: Mitral stenosis with or without insufficiency (38 patients) or pure insufficiency with thickened leaflets, calcified leaflets, chordal shortening, or chordal thickening (10 patients).
Degenerative: Pure mitral insufficiency with histological evidence of myxoid change (48 patients).
Bacterial endocarditis: Culture-positive endocarditis (3 patients).

Table 3 details the valve pathology.

Operative Technique

A similar operative technique was used throughout this experience, with the exception that before 1979 hypothermia and intermittent aortic cross-clamping was used for myocardial protection, whereas after 1979 St. Thomas' cardioplegic solution was used. The core temperature was always lowered to 25°C. Saphenous vein was used for coronary artery reconstruction in all the patients except in 2 in whom the left internal mammary artery was grafted to the left anterior descending artery. After the distal anastomoses were completed, the left atrium was opened through the interatrial groove. The mitral valve was examined and excised. The prosthesis was implanted using interrupted Dacron stitches with Teflon pledgets. The left atrium was then closed with 3-0 Prolene sutures. The aortic cross-clamp was released and proximal anastomoses were performed during rewarming.

Selection of valve prosthesis was based on patient's age, availability of postoperative anticoagulant therapy, and surgeon's preference. The types of prosthesis used are shown in Table 4. Table 5 shows the details of the coronary artery grafts.

Late Survival

Direct telephone contact of survivors was established in most patients. Annual questionnaire or office visits were used for those survivors who were not available for direct telephone contact. Cause of late death was assessed from hospital records and information from the patients' local medical officers and relatives.

Table 4. Valvar Prosthesis Selection and Hospital Mortality[a]

Prosthesis	No. of Patients	Deaths	Mortality (%)
Mechanical prosthesis			
Starr-Edward	106	12	11.32
Björk-Shiley	7	2	28.57
Medtronic	1	0	0
Bioprosthesis			
Carpentier-Edward	19	2	10.53
Hancock	2	0	0

[a] No significant difference between groups ($p = 0.674$).

Statistical Analysis

Univariate testing of variables was performed with χ^2 analysis or Fisher's exact test for discrete variables. Unpaired t test or one-way analysis of variance was used for continuous variables [10]. Stepwise multiple logistic regression analysis was then used to further test significant variables in a multivariate situation [10–12]. Any variables that had trends associating with death or survival ($p < 0.2$) were included in stepwise logistic multivariate regression analysis. Separate analyses were carried out for hospital or late deaths. Survival curves and standard errors were calculated by life-table methods [10, 13, 14]. Comparisons between actuarial survival curves were by the log-rank test [10]. Most calculations were computerized using Statview 512$^+$ software [15] in a Macintosh computer.

Results

Early Mortality

All the patients who died in the hospital were included in the early mortality. Sixteen patients died, an early mortality of 11.85%. Five patients died in the operating theater. Three patients died within 24 hours of operation. Eight patients died more than 24 hours postoperatively. The causes of in-hospital death were: low cardiac output, 7 patients; ventricular arrhythmia, 5; and respiratory failure, hemorrhage, stroke, and septicemia, 1 each. In 1 of the 7 patients who died of low cardiac output syndrome, low cardiac output was due to myocardial infarction (new Q waves on electrocardiogram). In 3 of the 5

Table 5. Number of Coronary Grafts and Hospital Mortality[a]

No. of Grafts	No. of Patients	Deaths	Mortality (%)
1	44	6	13.64
2	35	5	14.29
3	36	3	8.33
4	17	2	11.76
5	3	0	0

[a] No significant difference between groups ($p = 0.87$).

Table 6. Postoperative Situation and Hospital Mortality

Variable	No. of Patients	Deaths	Mortality (%)	p Value
Intubation				0.72
>24 hours	21	2	9.52	
<24 hours	114	14	12.28	
Renal failure				0.047
Yes	5	2	40	
No	130	14	10.77	
Catecholamines				0.09
Yes	50	9	18.0	
No	85	7	8.24	

patients who died of ventricular arrhythmia the arrhythmia was due to myocardial infarction.

Fifteen preoperative or operative variables were tested for the correlation to hospital mortality by univariate analysis. These results are listed in Tables 1–6. Of these variables, age, New York Heart Association (NYHA) functional class, number of diseased vessels, and WMS were significantly related to operative mortality ($p < 0.05$).

The variables that were significant in univariate analysis ($p < 0.05$) were included in the stepwise logistic multivariate regression to test if they were independent determinants. Preoperative atrial fibrillation and use of catecholamines in the intensive care unit postoperatively were also included in the multivariate regression because of their trend associating with hospital death ($p < 0.2$). The multivariate analysis demonstrated that WMS, preoperative NYHA functional class, and advanced age (>60 years) were independently associated with hospital mortality.

Hospital Morbidity

Four patients (2.9%) had perioperative myocardial infarction (new Q wave on electrocardiogram). Five patients had reoperation because of major hemorrhage within 24 hours after operation. Ventricular fibrillation developed in 3 patients in the early postoperative period, and 2 of them died. Atrial fibrillation developed in 61 patients postoperatively, and in 36 it was reverted before discharge; 25 patients were still in atrial fibrillation on discharge. Twenty-one patients had prolonged intubation (>24 hours). Five patients had renal failure requiring dialysis. A pulmonary embolus developed in 1 patient. Other serious morbidity included: ventricular tachycardia, 5 patients; bradycardia necessitating pacemaker insertion, 2 patients; atrial arrhythmia other than atrial fibrillation requiring treatment, 7 patients; cerebral vascular accident, 1 patient; temporary neurological injury, 3 patients; renal failure not requiring dialysis, 11 patients; severe respiratory dysfunction, 2 patients; and wound infection, 9 patients.

One hundred nineteen patients survived the operative hospitalization. Average hospital stay was 15.6 ± 0.1 days.

Late Results

One hundred nineteen patients survived hospitalization. Of the 119 hospital survivors, 115 patients were followed up. Four patients from overseas were lost to follow-up. The follow-up rate was 96.6%. Thirty-five patients subsequently died (late deaths). The causes of late deaths were: unknown, 11 patients; arrhythmia, 7; acute myocardial infarction, 6; stroke, 3; cardiac failure, 2; carcinoma, 2; and cardiac related but details unknown, traffic accident, embolic event, and valve problem, 1 each. New York Heart Association functional class of hospital survivors improved from an average of 3.41 preoperatively to 1.38 postoperatively (paired t test, $p < 0.001$). Of the survivors, 96.5% returned to their previous employment. Three patients had their mitral valve prosthesis replaced subsequently, and 10 patients (8.9%) had a return of angina.

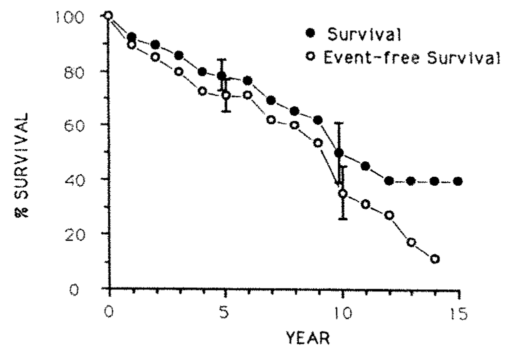
In univariate analysis, tested for correlation with late death were: sex, age (older than 60 years), preoperative cardiac enlargement, atrial fibrillation, interval between recent myocardial infarction and operation, number of previous infarctions, Canadian Heart Class related to angina, number of diseased vessels, preoperative NYHA functional class, mitral regurgitation, low cardiac index (<1.5 L/m^2), WMS, valve pathology, type of valve prosthesis, number of grafts, use of catecholamines postoperatively, and intubation for more than 24 hours. Of these variables, cardiac enlargement, number of diseased vessels (double-vessel or left main artery disease), preoperative NYHA functional class (III or IV), and use of catecholamines postoperatively significantly increased late mortality ($p < 0.05$). These variables were included in a multivariate regression analysis. Preoperative Canadian Heart Class, type of valve prosthesis, and prolonged intubation were also included in the multivariate regression analyses because of the trend associating with late deaths ($p < 0.2$). The multivariate regression analysis demonstrated that preoperative NYHA functional class and use of catecholamines postoperatively were independently associated with late deaths.

Survivors were followed up from 1 month to 174 months. Mean follow-up was 52.6 ± 4.1 months. Survival probability was 91.9%, 89.9%, 78%, and 49.9% at 1, 2, 5, and 10 postoperative years, respectively (Fig 1). Figure 1 also shows event-free survival, which excluded the patients who had angina, acute myocardial infarction, or reoperation because of valve dysfunction.

Figure 2 shows survival in patients with ischemic, degenerative, and rheumatic valvar pathology. There was no significant difference between these three groups ($p > 0.05$).

Figure 3 shows survival of patients with single-, double-, triple-vessel, and left main coronary artery disease. There was a significant difference between these four groups ($p < 0.01$). Preoperative NYHA functional class was closely related to long-term survival. Figure 4 show survival of patients in NYHA class I/II, III, or IV. There was a significant difference between these three groups ($p < 0.025$).

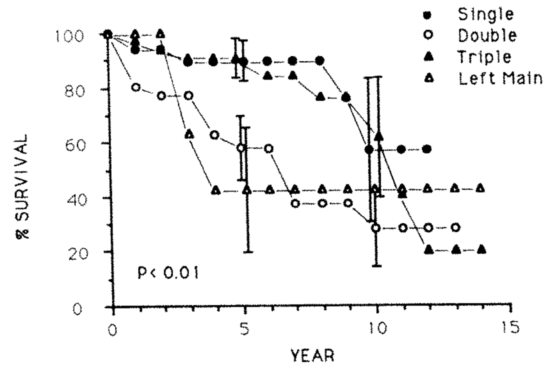
Figure 5 shows survival of patients with different de-



Number At Risk

Survival	119	48	10	1
Event-free Survival	119	47	9	0

Fig 1. Survival and event-free survival after combined mitral valve replacement and coronary artery bypass grafting.



Number At Risk

Single	35	17	2	0
Double	33	11	3	0
Triple	38	17	3	0
Left Main	9	2	1	0

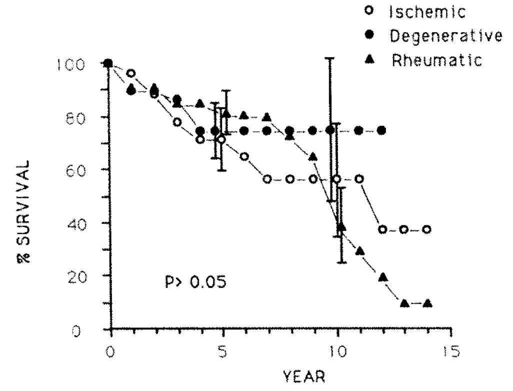
Fig 3. Survival after combined mitral valve replacement and coronary artery bypass grafting according to number of diseased vessels. Five-year survival was 89.7%, 57.4%, 90.7%, and 42.4% in the patients with single-, double-, triple-vessel, and left main artery disease, respectively.

grees of mitral regurgitation preoperatively. There was no significant difference between these three groups ($p > 0.25$).

Figure 6 shows survival of patients who received and those who did not receive catecholamine therapy in the intensive care unit postoperatively. There was a significant difference between these two groups ($p < 0.025$).

Comment

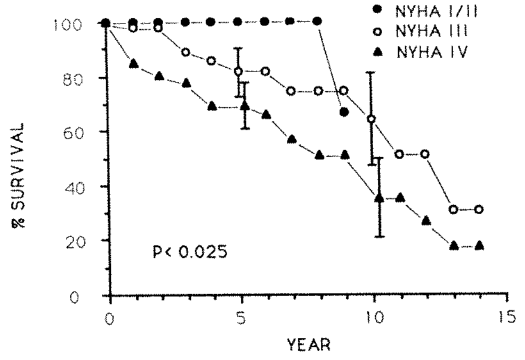
Most institutions have reported that the mortality for combined MVR and CABG is greater than for either MVR or CABG [16], indicating that the combination of mitral disease (either incompetence or stenosis) and coronary artery disease is a serious circumstance. This is also demonstrated in the present study. In this study, 91.9% (124/135) of our patients were in NYHA functional class III or IV preoperatively (see Table 1). Ischemic mitral valve disease was thought to have a higher risk than other etiological factors [16], and this was demonstrated in a study by Czer and associates [5]. On the other hand, in a study by Lytle and co-workers [4], etiological factors were not related to early mortality, but they were related to late survival: patients with degenerative mitral disease had superior survival compared with other groups. Nevertheless, only little information has been available to determine the operative and long-term survival. We divided our patients into four groups—ischemic, degenerative, rheumatic, and infective disease—by strict criteria [4]. Our results show that there were no differences between these groups in either hospital mortality or long-term survival. In our study, most of the patients (66.7%, 24/36)



Number At Risk

Ischemic	28	11	3	0
Degenerative	40	16	2	0
Rheumatic	47	20	4	0

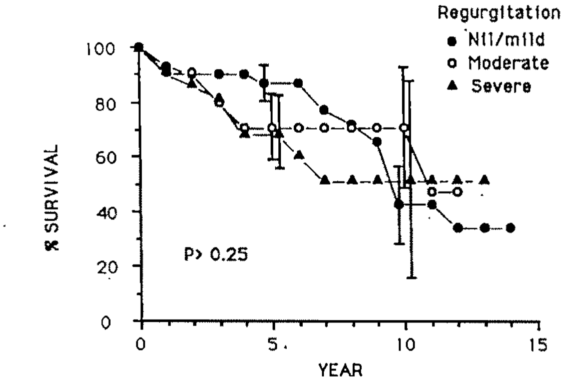
Fig 2. Survival after combined mitral valve replacement and coronary artery bypass grafting according to cause of mitral valve disease. Five-year survival was 71.4%, 74.6%, and 80.7% in the ischemic, degenerative, and rheumatic groups, respectively.



Number At Risk

NYHA I/II	11	5	0	0
NYHA III	50	20	5	0
NYHA IV	54	22	4	0

Fig 4. Survival after combined mitral valve replacement and coronary artery bypass grafting according to New York Heart Association (NYHA) functional class. Five-year survival was 100%, 81.4%, and 69.3% in patients in class I/II, III, and IV, respectively.



Number At Risk

	0	5	10	15
Nil/mild	58	25	5	0
Moderate	33	13	3	0
Severe	24	9	1	0

Fig 5. Survival after combined mitral valve replacement and coronary artery bypass grafting according to magnitude of mitral regurgitation. Five-year survival was 86.8%, 70.7%, and 68.9%, respectively, in patients with nil/mild, moderate, and severe regurgitation.

in the ischemic group had previous infarctions that caused the mitral regurgitation, and these patients had recovered from their previous infarctions by the time they were operated on. Lytle and colleagues [4] found similar results in their study even though their ischemic group had fewer patients (27.7%, 13/47) whose mitral regurgitation was caused by previous infarctions. In their study, they also found that the etiological factors were not correlated with early mortality.

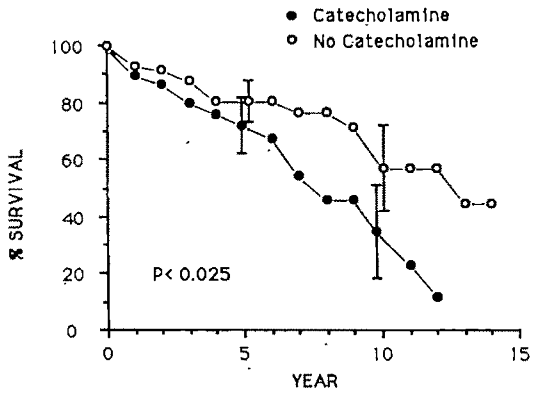
Pinson and colleagues [6] demonstrated that the severity of ischemic mitral regurgitation was related to long-term survival. There is little information available regarding correlation between long-term survival and severity of mitral regurgitation due to other causes in the patients who have had mitral valve replacement combined with CABG. We divided our patients into three groups according to the severity of the mitral regurgitation (without or with only mild regurgitation, with moderate regurgitation, and with severe regurgitation) with either cause. In the group without or with only mild regurgitation (68 patients) most of these patients had MVR for mitral stenosis (see Table 3). We found that there was no significant correlation between the severity of the mitral regurgitation and either hospital or late survival ($p > 0.05$). There was also no difference between hospital mortality in the patients who had mitral stenosis and the patients who had only mitral regurgitation.

In this study, age is a determinant of early mortality for combined MVR and CABG. The hospital mortality for patients older than 60 years was 16.3%, compared with only 4.1% in patients younger than 60 years old ($p \leq 0.05$).

Preoperative cardiac function is an important determinant of hospital mortality. Our results showed that there were no deaths in patients in NYHA class I or II preoperatively. In patients who were in NYHA class III, the mortality increased to 5.5%, whereas in patients in NYHA class IV, the mortality was 18.8% ($p < 0.05$ between these three groups). The effects of preoperative cardiac function on hospital mortality were also demonstrated in the correlation between WMS and mortality. In the patients with normal or mildly impaired left ventricular contraction indicated by a WMS of 5 to 10, the mortality was 5.7%, whereas in the patients with moderately impaired left ventricular contraction (WMS, 11 to 15), the mortality increased to 26.7%. We had only 2 patients in the category of severely impaired left ventricular contraction; 1 of them died ($p < 0.025$, between the three groups). The average WMS was 11.1 ± 1.6 in 8 patients who died and 8.3 ± 0.3 in 62 hospital survivors ($p < 0.01$). This study clearly indicates that WMS is a useful index to predict operative risk for patients who may undergo combined MVR and CABG. As WMS and NYHA functional class are associated with each other, being indices of cardiac function, the effects of WMS and NYHA functional class on hospital mortality were similar in this study. We presume that cardiac function is a factor more directly related to mortality than is mitral regurgitation. Even in those patients operated on under emergency circumstances (acutely ruptured papillary muscle in 6 patients and infarcted papillary muscle in another 6 patients) there were no operative deaths (see Table 3) because the cardiac function in these patients was still reasonable regardless of the development of acute mitral regurgitation.

Our results also indicated that patients who had left main artery disease had greater hospital mortality (35.7%, $p = 0.027$) (see Table 2).

Variables relating to operation such as type of valve prosthesis and number of coronary artery grafts have been tested regarding their correlation to operative mortality [5], and little correlation was found between these variables and operative mortality. Our policy is always to attempt complete revascularization, and we think this was the reason why the number of vessels grafted was not



Number At Risk

	0	5	10	15
Catecholamine	40	17	3	0
No Catecholamine	75	30	6	0

Fig 6. Survival after combined mitral valve replacement and coronary artery bypass grafting according to use of catecholamines postoperatively in the intensive care unit. Five-year survival was 72.0% for patients who received catecholamine therapy and 80.4% for patients who did not receive catecholamine therapy.

correlated with the operative mortality in our experience (see Table 5). Others have demonstrated that incomplete coronary revascularization is correlated with operative mortality [17].

Five-year survival after MVR and CABG has been reported as 69% [6], 66% [4], and 31.3% [3]. Mitral valve pathology, anticoagulant therapy [4], left ventricular end-diastolic volume, left ventricular ejection fraction [5], and severity of mitral valve regurgitation [6] have been suggested to be predictors of long-term survival. However, only a few reports are available, and in these reports, the effects of preoperative or operative variables are contradictory. In our study, univariate analysis demonstrated that heart enlargement, number of diseased vessels, preoperative NYHA functional class, and use of catecholamines were significantly related to late survival. We also looked at the effects of valve pathology, number of diseased vessels, severity of mitral regurgitation, NYHA functional class, cardiac index, and WMS on long-term survival using life-table methods. We found that only the number of diseased vessels, preoperative NYHA functional class, and use of catecholamines postoperatively were correlated with survival ($p < 0.01$, $p < 0.025$, and $p < 0.025$, respectively). In the group of patients who had left main artery disease the 5-year survival was only 42.4%, compared with 89.4%, 57.4%, and 90.0% in the groups with one-, two-, or three-vessel disease ($p < 0.01$ between these four groups). The patients who were in NYHA class IV had a 5-year survival of 69.3%, compared with 100% and 81.4% in the groups of patients who were in NYHA class I/II or III ($p < 0.025$ between these three groups). Those patients who received catecholamine therapy postoperatively had a 5-year survival of 72.0%, compared with 80.4% in the patients who did not receive catecholamine therapy ($p < 0.025$).

In this study, we could not find effects of cause and pathology of mitral valve disease on hospital or long-term survival. This should not be interpreted as demonstrating that myocardial ischemia has no effect on survival because all of the 135 patients in this study had coronary disease and needed coronary bypass grafts. What we think should be emphasized is that etiological and pathological factors of mitral valve disease in this particular group of patients do not seem to have effects on survival. On the other hand, severity of myocardial ischemia does have effects on survival because NYHA functional class and WMS are indices for survival as already mentioned.

We did not find any difference in survival according to the cause of valve disease, valve pathology, severity of mitral valve regurgitation, or low cardiac index in this study. This encourages us to operate on those patients who have coronary artery disease and mitral valve disease regardless of the cause of the mitral valve disease or the severity of the mitral regurgitation. However, we now avoid surgical intervention on the mitral valve if the mitral regurgitation is mild or moderate, believing this, as has been indicated by others [3], may not compromise operative results. We also try to repair the mitral valve in select patients now.

In conclusion, our study suggests that satisfactory long-term survival can be obtained after combined MVR and CABG regardless of the cause of mitral valve disease or the severity of mitral regurgitation, and that preoperative NYHA functional class is the most important predictor for both hospital mortality and long-term survival.

We thank Mrs Sonja E. Hall and Mr Robert Beetson for their assistance in reviewing and collecting the clinical data.

References

1. Gahl K, Sutton R, Pearson M, Caspari P, Lairet A, McDonald L. Mitral regurgitation in coronary heart disease. Br Heart J 1977;39:13–8.
2. Balu V, Hershowitz S, Zaki Masud AR, Bhayana JN, Dean DC. Mitral regurgitation in coronary artery disease. Chest 1982;81:550–5.
3. Arcidi JM, Hebeler RF, Craver JM, Jones EL, Hatcher CR, Guyton RA. Treatment of moderate mitral regurgitation and coronary disease by coronary bypass alone. J Thorac Cardiovasc Surg 1988;95:951–9.
4. Lytle BW, Cosgrove DM, Gill CC, et al. Mitral valve replacement combined with myocardial revascularization: early and late results for 300 patients, 1970 to 1983. Circulation 1985; 71:1179–90.
5. Czer LSC, Gray RJ, DeRobertis MA, et al. Mitral valve replacement: impact of coronary artery disease and determinants of prognosis after revascularization. Circulation 1984; 70(Suppl 1):198.
6. Pinson CW, Cobanoglu A, Metzdorff MT, Grunkemeier GL, Kay PH, Starr A. Late surgical results for ischemic mitral regurgitation. Role of wall motion score and severity of regurgitation. J Thorac Cardiovasc Surg 1984;88:663–72.
7. Kennedy JW, Kaiser GC, Fisher LD, et al. Clinical and angiographic predictors of operative mortality from the Collaborative Study in Coronary Artery Surgery (CASS). Circulation 1981;63:793–802.
8. CASS principal investigators and their associates. Coronary Artery Surgery Study (CASS): A randomized trial of coronary bypass surgery. Quality of life in patients randomly assigned to treatment groups. Circulation 1983;68:951–60.
9. Killip T, and the principal investigators of CASS. The national Heart, Lung, and Blood Institute Coronary Artery Surgery Study (CASS). Circulation 1981;63(Suppl 1):1–81.
10. Armitage P, Berry G. Statistical methods in medical research. 2nd ed. London: Blackwell Scientific, 1987.
11. Cox DR, Snell EJ. Analysis of binary data. 2nd ed. New York: Chapman and Hall, 1989.
12. Manly BFJ. Multivariate statistical methods. New York: Chapman and Hall, 1988.
13. Anderson RP, Boncheck LI, Grunkmeier GL, Lambert LE, Starr A. The analysis and presentation of surgical results by actuarial methods. J Surg Res 1974;16:224–30.
14. Grunkemeier LG, Starr A. Actuarial analysis of surgical results: rationale and method. Ann Thorac Surg 1977;24: 404–8.
15. Statview 512$^+$. Calabasas CA: Brain Power, Inc, 1986.
16. Karp RB. Mitral replacement and coronary artery bypass grafting. Ann Thorac Surg 1982;34:480–1.
17. DiSesa VJ, Cohn LH, Collins JJ, Koster JK, VanDevanter S. Determinants of operative survival following combined mitral valve replacement and coronary revascularization. Ann Thorac Surg 1982;34:482–9.

DISCUSSION

DR CARY J. LAMBERT (Dallas, TX): I wish to mention an approach altogether different, first suggested to me by Robert Flemma, that is suitable for both mitral and aortic valve disease associated with coronary artery disease. The idea is to place the grafts onto the coronary arteries first and then onto the aorta. The clamp across the aorta is then moved proximal to those grafts. The grafts are then functional, and the valve is approached with the heart being completely perfused from the bypass system. This way there is considerably less mortality.

The other advantage of this technique is when one is using a ring to correct valvar insufficiency, because it provides a method for precise examination of the valvoplasty without a probability of embolization.

DR DAVID GALBUT (Miami, FL): One of your conclusions that the use of catecholamines has an influence on long-term survival may reflect more the left ventricular function preoperatively. As cardiac surgeons, we all tend to use catecholamines at different thresholds for different reasons. The way I would interpret those results is that you used catecholamines in the patients with the worst preoperative or postoperative ventricular function, as opposed to having an effect of the use of catecholamines per se.

DR HE: Yes, that is a very interesting question. The catecholamines were used in these patients for their inotropic effects hemodynamically. The patients who had received catecholamines postoperatively had the worse long-term survival. That could be, as you just mentioned, related to the preoperative heart function. Also, it could be related to the preservation of myocardium and left ventricular function. We have found that there is a relationship between use of catecholamines and survival. We did not recommend when to use or not use catecholamines in this category of patients.

DR DENIS H. TYRAS (New Hyde Park, NY): I wonder, in your operative technique, whether you made efforts to preserve the valve or whether your standard technique is to excise the valve, because of the serious influence that this has on postoperative left ventricular function. I also wonder if you have some assessment of postoperative left ventricular function.

Based on some of the pioneering work by Dick Clark, we have made extensive efforts during the last year to preserve the entire mitral valve mechanism during mitral valve replacement. When we look back at our patients who underwent mitral valve replacement in 1989, three quarters of whom had concomitant coronary bypass grafting, in 10 of those 13 patients the postoperative ejection fraction was lower than that seen preoperatively. In contrast, during 1990, we have operated on 10 patients who all have had postoperative ejection fractions of anywhere from 0.50 to 0.65. Preoperatively, only half of those patients had normal ejection fractions.

I think that your operative mortality and some of your late results may be related to the lack of preservation of the mitral valve mechanism rather than any damage to the myocardium from inadequate myocardial preservation. Would you address that?

DR HE: We did not try to preserve the mitral apparatus before, but we do it now. Related to your question is the fact that we also started doing more mitral valve repairs recently. This work goes out to 1989. After that, we started to do more repairs. For the patients with moderate regurgitation, we now attempt repair as the procedure of choice.

Enhanced Pulmonary Function Using Dimethylthiourea for Twelve-Hour Lung Preservation

C. Jake Lambert, Jr, MD, Thomas M. Egan, MD, Frank C. Detterbeck, MD, Blair A. Keagy, MD, and Benson R. Wilcox, MD

Division of Cardiothoracic Surgery, University of North Carolina School of Medicine, Chapel Hill, North Carolina

Current preservation techniques for lung transplantation limit ischemic time to 6 hours. The purpose of this study was to evaluate the ability of dimethylthiourea, a low molecular weight free radical scavenger, to prolong this interval. An in vivo canine transplantation model was used to assess lung function. At harvest and after circulatory arrest, the donor lung was flushed with modified Euro-Collins solution (50 mL/kg). In a blinded fashion, dimethylthiourea (5 g) or saline solution was added to the flush solution at harvest and also infused (20 g over 2 hours) at reimplantation. Harvested lungs were stored for 12 hours at 4°C. Allotransplantation was performed in recipient dogs ventilated with 40% O_2. After 1 hour, the contralateral pulmonary artery was ligated, forcing the dog to be dependent on the transplanted lung. Twelve dogs were studied, with 6 randomly assigned to each treatment group in a blinded fashion. Measurements were recorded for 8 hours, keeping the inspired oxygen fraction constant at 0.40. All dimethylthiourea-treated dogs survived the observation period, whereas one third of the dogs that received saline solution died. Dimethylthiourea-treated dogs had significantly greater arterial oxygen tension and significantly less pulmonary vascular resistance compared with control animals. These results suggest that treatment of the lung with a free radical scavenger (dimethylthiourea) improves pulmonary function after reimplantation in a canine model after 12-hour hypothermic storage.

(Ann Thorac Surg 1991;51:924–30)

Despite attempts with various preservation techniques, the safe ischemic time for lung transplantation is still limited to less than 6 hours. The ability to extend this interval to up to 12 hours would provide many benefits including increasing the number of organs available for transplantation, enhancing the ability to share organs between centers, improving the overall logistics of transplantation, and possibly allowing HLA histocompatibility matching between donor and recipient before transplantation [1].

Transplanted organs are injured from events that occur during ischemia and reperfusion. Such injury or "reimplantation response" is characterized by pulmonary edema, increased pulmonary vascular resistance, and hypoxemia after lung transplantation. Evidence continues to accumulate that at least part of this response is due to the formation of oxygen free radicals [2–5]. Free radical–mediated injury after ischemia and reperfusion has been reported in other organs including heart [6], liver [7], kidney [8], pancreas [9], brain [10], intestine [11], and muscle [12].

We recently demonstrated attenuation of lung injury after 24-hour hypothermic preservation using an in vivo, nonsurvival canine allotransplantation model by treatment with the oxygen free radical scavenger dimethylthiourea (DMTU). This study demonstrated lower pulmonary artery pressures and improved early oxygenation in DMTU-treated animals compared with controls [13]. However, continued deterioration of pulmonary function occurred late during the follow-up period and may be due to irreversible damage to the lungs with 24-hour storage. This study was undertaken to determine the effect of DMTU on early lung function after 12-hour hypothermic storage.

Material and Methods

Reagents and Equipment

Sodium pentobarbital was purchased from Barber Veterinary Supply of Richmond, VA. Prostaglandin E_1 and α-chloralose were purchased from Sigma Chemicals Co, St. Louis, MO. *N,N'*-dimethylthiourea was obtained from ICN Biomedicals, Cleveland, OH. Cefazolin was purchased from Eli Lilly Co of Indianapolis, IN, and sodium heparin was obtained from Elkins Sinn Co in Cherry Hill, NJ.

American Edwards Laboratories of Irvine, CA, manufactured the Swan-Ganz catheters, the femoral artery lung water catheters, and the Lung Water Computer. Transducer-derived pressures and cardiac outputs were recorded using a BNC to 34-pin ribbon cable interface on an Apple Macintosh II microcomputer.

Presented at the Thirty-seventh Annual Meeting of the Southern Thoracic Surgical Association, Dorado, Puerto Rico, Nov 8–10, 1990.

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Anesthesia

Heartworm-negative, adult mongrel dogs were weighed and anesthetized with 30 mg/kg of intravenous sodium pentobarbital. Each recipient was matched to within 10% of the donor's weight. Anesthesia was maintained in the recipient dogs by infusing α-chloralose (12.5 $mg \cdot kg^{-1} \cdot h^{-1}$) 1 hour after the initial pentobarbital dose. Animals were ventilated with a tidal volume of 15 mL/kg. Donor dogs were ventilated with room air, whereas recipients received 40% oxygen.

Harvest

Harvest and transplantation methods were performed as described in a previous publication [13]. After induction of anesthesia in donors, left thoracotomy was performed and all hilar structures were isolated. The main pulmonary artery (PA) was cannulated with a 24F catheter. Animals were heparinized before ligation of the right PA. One milligram of prostaglandin E_1 in 50 mL of normal saline solution was infused through the PA catheter over a 3- to 4-minute period. Blood pressure was monitored, and the infusion rate was adjusted so that systemic hypotension did not occur.

The left side of the heart was then vented by incision of the left atrial appendage. The inflow to the main PA was occluded. The lung was perfused over a 3- to 4-minute period with 50 mL/kg of modified Euro-Collins solution that had been stored at 4°C. The composition of the solution was as follows: K_2HPO_4, 7.40 g; $NaHCO_3$, 0.84 g; KHPO, 2.04 g; KCl, 1.12 g; $MgSO_4$, 0.48 g; cefazolin, 1.00 g; D50W, 50 mL, and heparin, 5,000 U. The osmolality was 326 mOsm/kg; with DMTU added, the osmolality was 371 mOsm/kg. Ventilation was continued with room air, and the flow rate was adjusted so that the PA pressure stayed less than 20 mm Hg.

At completion of the flush, the left lung was excised, including a small cuff of left atrium. The lung was then inflated with 100% N_2 at a pressure of 25 to 30 cm H_2O before the bronchus was clamped. The lung was submerged in Euro-Collins solution and stored for 12 hours at 4°C. The harvest time was defined as the time from the onset of flushing until the lung was submerged in solution.

Transplantation

One gram of cefazolin was administered to recipient animals after induction of anesthesia. A right femoral arterial line was placed before a Swan-Ganz catheter was advanced from the right femoral vein. Left thoracotomy was performed and all hilar structures were isolated. The contralateral PA and bronchus were encircled with umbilical tape tourniquets. A Millar pressure transducer was placed in the left atrium. The contralateral PA and bronchus were occluded using the tourniquets after heparinization. An electromagnetic flow probe was placed around the left PA. After 5 minutes, baseline measurements of the native lung were recorded.

The donor lung was removed from storage, deflated, and wrapped in iced soaked saline sponges. Allotransplantation was performed in a manner similar to the method described by Hardy and colleagues [14]. Left atrial horizontal mattress anastomosis was performed first, using 5-0 Prolene (Ethicon, Somerville, NJ). The bronchial ends were anastomosed with running 4-0 Prolene. 6-0 Prolene was used for the PA anastomosis. Before completion of the PA suture line, the PA was flushed to remove air. The transplantation time was defined as the time from removal of the lung from storage until blood flow was restored to the organ. "Warm ischemic time" was considered as the harvest time plus the transplantation time.

Experimental Groups

A vial containing 50 mL of either DMTU (5 g in saline solution) or saline solution was added to the flush solution. An infusion of 50 mL of DMTU (20 g in normal saline solution) or saline solution was begun just before reperfusion of the transplanted lung and continued for 2 hours. The flush and infusion solutions were administered in a blinded fashion. Twelve transplantations were performed: half of the animals (n = 6) were given saline solution (controls) and 6 were administered DMTU.

Measurements

After 1 hour, the contralateral PA and bronchus were ligated, forcing the recipient to be completely dependent on the transplanted lung. The tidal volume was decreased by half and the respiratory rate was doubled to maintain adequate ventilation. The inspired oxygen concentration was kept constant at 0.40 during the follow-up period. The ventilatory rate was adjusted as needed to keep the carbon dioxide tension between 35 and 45 mm Hg. If metabolic acidosis occurred, intravenous sodium bicarbonate was infused to maintain pH from 7.35 to 7.40. Ringer's lactate was used for intravenous fluid. Fluid restriction was instituted, with the left atrial pressure maintained from 5 to 10 mm Hg. Interventions were not made within 15 minutes of measurements.

A Doppler flow probe was placed on the left PA, and the chest was closed loosely. Hemodynamic recordings of the PA, aorta, distal trachea, left atrium, and right atrium were taken every hour for the 8-hour follow-up period. In addition, an Edwards Lung Water Computer was used to estimate the extravascular lung water by the thermal-thermal method. Survivors of the follow-up period were sacrificed. After death, the transplanted lung was harvested and weighed.

Statistics

Hemodynamic and pulmonary function data were collected hourly. Data from 2 consecutive hours were pooled for comparison between groups. The results were presented as mean ± standard error of the mean. Differences between groups were evaluated using unpaired *t* tests. Chi square analysis was used to compare survival between treatment groups. Differences were considered significant at the *p* less than 0.05 level.

The Institutional Animal Care and Use Committee of the University of North Carolina reviewed and approved the protocol for this study. All animals received humane

Table 1. Comparison of Experimental Groups[a]

Variable	Control	DMTU
Animal weight (kg)	22.1 ± 1.5	22 2 ± 1.1
Harvest time (min)	11.3 ± 1.0	10.3 ± 0.7
Warm ischemia (min)	74.3 ± 4.6	70.3 ± 0.7
Preservation (h)	13.1 ± 0.2	13.2 ± 0.4

[a] There are no significant differences between the control and DMTU groups.

DMTU = dimethylthiourea.

care in accordance with the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985).

Results

Groups were similar with regard to animal weights, harvest time, preservation time, and "warm" ischemic time (Table 1). All the DMTU-treated animals survived the observation period, whereas 2 of the 6 control animals died at 3 and 6 hours after completion of the transplantation. Survival was not significantly different (p = not significant) by Fisher's exact test. No differences in PA pressure (Fig 1), extravascular lung water, or left atrial pressure were demonstrated between treatment groups during the 8-hour follow-up period.

Lung function appeared improved in the DMTU-treated animals. The arterial oxygen tensions for the DMTU-treated animals were greater. However, the differences were significant for the first 4 hours only (Fig 2). Similarly, the percent arterial oxygen saturation was significantly less (Fig 3) in controls for the first 6 hours. Pulmonary vascular resistance was significantly less in the DMTU treatment group (Fig 4). In addition, central venous pressures were less with DMTU therapy. The differences were significant for the first 4 hours (Fig 5). The calculated intrapulmonary shunt fraction was significantly greater in control animals for the first 4 hours (Fig 6) but not later.

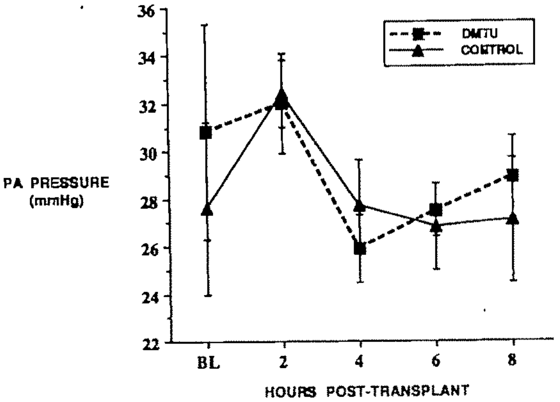

Fig 1. Pulmonary artery (PA) pressure versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

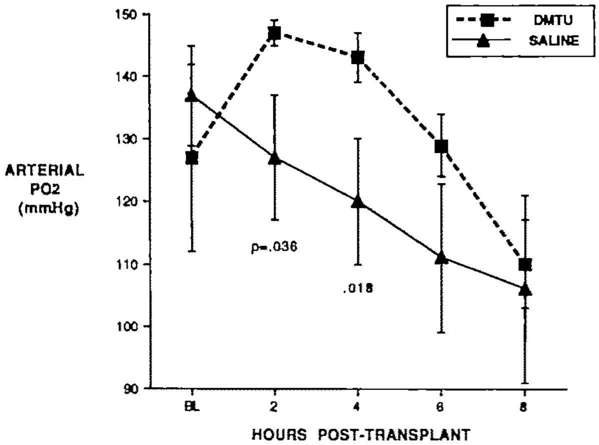

Fig 2. Arterial oxygen tension (PO2) versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

The DMTU treatment group also demonstrated improved hemodynamic function compared with controls. The mean aortic pressures were significantly less in the DMTU treatment group throughout follow-up (Fig 7). In addition, cardiac outputs were significantly greater with the DMTU-treated dogs at all intervals (Fig 8). Systemic vascular resistance (Fig 9) was significantly less in the DMTU group at all intervals. The mixed venous oxygen tensions were significantly greater in the DMTU group at 4 and 6 hours after transplantation (Fig 10).

Comment

Organs preserved for transplantation are injured from events that occur during ischemia and subsequent reperfusion. At least part of this injury results from the production of toxic metabolites of oxygen, ie, oxygen free radicals [1–5, 15–17]. Mechanisms of oxygen free radical formation include xanthine oxidase, neutrophils, arachidonic acid, and mitochondria [2, 16, 17]. Oxygen free

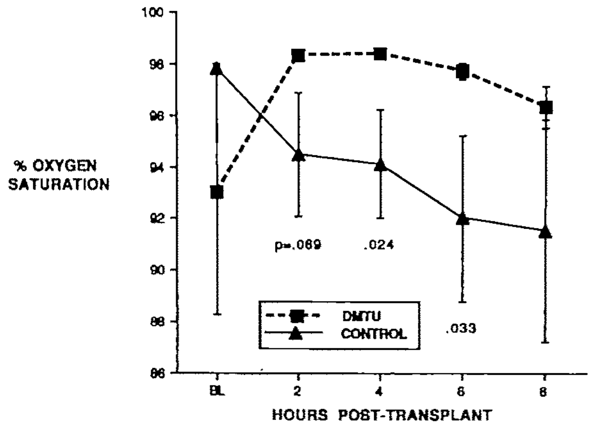

Fig 3. Percent arterial oxygen saturation versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

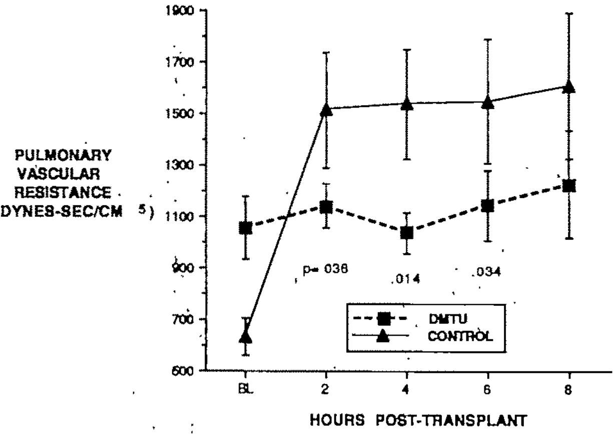

Fig 4. Pulmonary vascular resistance versus time after transplantation. (BL = baseline; DMTU *= dimethylthiourea.)*

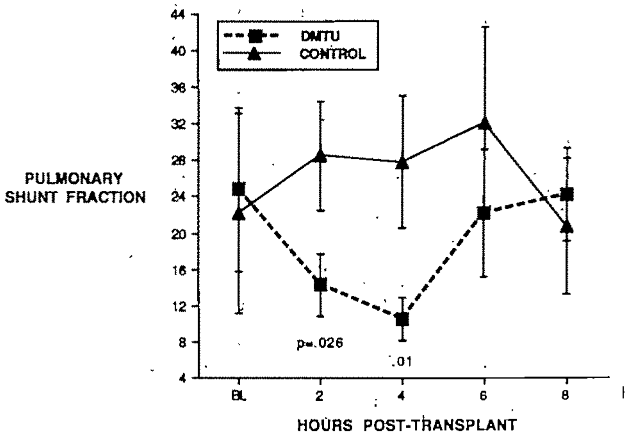

Fig 6. Intrapulmonary shunt fraction versus time after transplantation. (BL = baseline; DMTU *= dimethylthiourea.)*

radicals such as superoxide radicals, hydrogen peroxide, and hydroxyl radicals are formed during events of ischemia and reperfusion.

Hydroxyl radicals react with polyunsaturated lipid membranes to form lipid radicals [16, 17]. Lipid radicals, like all free radicals, can act as oxidants or reducing agents and thus can propagate the formation of other lipid radicals. This lipid peroxidation results in increased cell membrane permeability and ultimately in pulmonary edema in a reperfused lung [18]. The primary site of such ischemia and reperfusion injury appears to be the vascular endothelial cell [19].

There is mounting evidence that oxygen free radical scavengers can lessen reperfusion injury. Cremer and associates [20] demonstrated improved oxygenation in lungs flushed with Euro-Collins solution and superoxide dismutase/catalase compared with Euro-Collins solution alone using an in vivo, nonsurvival model. Bando and co-workers [21] demonstrated improved lung function with decreased pulmonary vascular resistance and extravascular lung water using superoxide dismutase with an in vivo model of heart-lung transplantation after 12-hour preservation. Recently, the addition of both allopurinol and deseroxamine to the flush solution of lungs stored for 4 hours was shown to improve subsequent lung function [22]. Dimethylthiourea, a potent hydroxyl radical scavenger, has been shown to attenuate reperfusion-mediated injury in in vitro investigations [23–25]. However, Bishop and associates [26] did not demonstrate any improvement in lung function using DMTU after a 48-hour ischemic interval.

In vitro studies from our lab using an isolated, perfused lung model also demonstrated improved pulmonary function with resultant decreases in PA pressure, pulmonary vascular resistance, and extravascular lung water by the protective cellular enzymes superoxide dismutase and catalase [27, 28]. Further in vitro studies in this laboratory using DMTU documented improved hypothermic lung preservation by reducing lipid peroxidation and edema formation on reperfusion in a isolated perfused lung model [18].

Dimethylthiourea has several properties that are advantageous for use in transplantation. In addition to having no reported toxic effects, DMTU is a low molecular weight

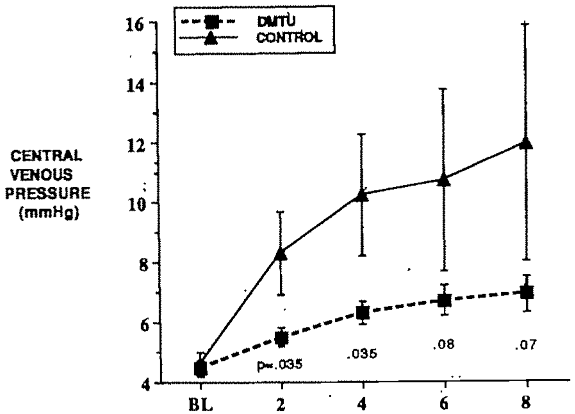

Fig 5. Central venous pressure versus time after transplantation. (BL = baseline; DMTU *= dimethylthiourea.)*

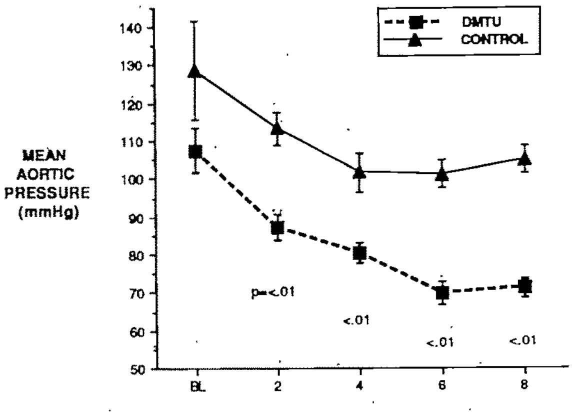

Fig 7. Mean aortic pressure versus time after transplantation. (BL = baseline; DMTU *= dimethylthiourea.)*

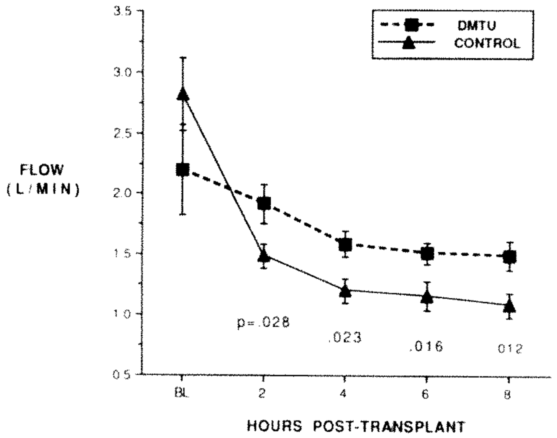

Fig 8. Cardiac output versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

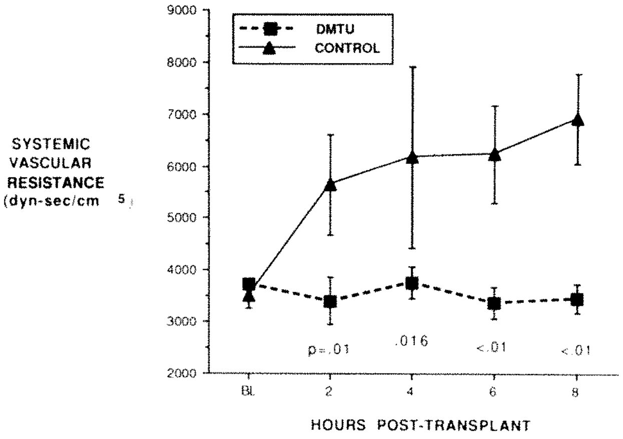

Fig 9. Systemic vascular resistance versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

compound, which allows it to diffuse rapidly across cell membranes [29]. Dimethylthiourea has a relatively long half-life of 28 to 36 hours, which should allow it to remain in tissue during the storage interval. In vitro studies have shown that DMTU is a potent scavenger of hydroxyl radicals that will also react with H_2O_2 and HOCl but not superoxide [24, 25].

It is possible that some of the beneficial effects noted with DMTU administration are related to the different osmolality of the solutions. Its ability to diffuse across cell membranes may preclude this being a substantial effect.

Our previous study [13] of 24-hour lung preservation using the same in vivo model to study acute pulmonary function demonstrated lower PA pressures and improved oxygenation early after transplantation. However, progressive deterioration of lung function occurred during the follow-up period. We postulated that this deterioration was due to the severity of the lung injury that occurs with 24-hour hypothermic storage. The current study was performed with the preservation time decreased to 12 hours and administering DMTU or saline solution in a blinded fashion.

This study documented improved pulmonary function in the DMTU-treated dogs with 12-hour hypothermic storage. Although there was no difference in mean PA pressure or extravascular lung water after transplantation, significant improvement in arterial oxygen tension, central venous pressure, cardiac output, pulmonary vascular resistance, and intrapulmonary shunt fraction was documented. In addition to the pulmonary effects, the DMTU-treated animals had improved hemodynamics. Dimethylthiourea therapy resulted in increased cardiac output, increased mixed venous oxygenation, decreased mean arterial pressure, and improved survival. The elevated central venous pressure in control animals implies increased right heart dysfunction probably related to the increased pulmonary vascular resistance.

A loss of statistical significance in some variables at later time points is a consequence of (1) greater variability in some physiologic parameters in the control animals (cf Fig 5) and (2) the death of 2 of the control dogs, resulting in fewer measurements for comparison at these hours. Some deterioration in lung function with time did occur in both groups. It is conceivable that the benefit of DMTU would not be sustained with longer follow-up. This possibility has not been excluded by this study and may account for the loss of statistical significance at later time points.

Pulmonary function consistently appeared very good in DMTU-treated animals. Flushing the lungs with modified Euro-Collins solution alone provided variable lung preservation in our controls. Two control animals had pulmonary function that was as good as that of the DMTU-treated animals. However, 2 control animals that died had poor lung function, and the remaining 2 controls demonstrated marginal lung function.

In summary, our blinded study in an in vivo allotransplantation model demonstrated enhanced early pulmonary function and improved hemodynamics after 12-hour hypothermic preservation using the oxygen free radical scavenger DMTU. Further studies are needed to assess late pulmonary function and to determine whether bronchial healing will be adequate after such preservation.

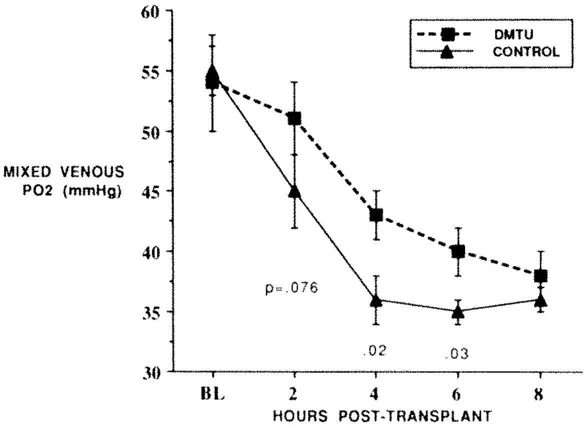

Fig 10. Mixed venous oxygen tension (PO2) versus time after transplantation. (BL = baseline; DMTU = dimethylthiourea.)

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References

1. Egan TM, Kaiser LR, Cooper JD. Lung transplantation. Curr Probl Surg 1989;26:673–752.
2. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 1985;312:159–63.
3. Grosso MA, Brown JM, Viders DE, et al. Xanthine oxidase-derived oxygen radicals induce pulmonary edema via direct endothelial cell injury. J Surg Res 1989;46:355–60.
4. Tate RM, Vanbenthuysen KM, Shasby DM, et al. Oxygen-radical–mediated permeability edema and vasoconstriction in isolated perfused rabbit lungs. Am Rev Respir Dis 1982; 126:802–6.
5. Linas SL, Whittenburg D, Repine JE. Role of xanthine oxidase in ischemia/reperfusion injury. Am J Physiol 1990;27: F711–6.
6. Zweier JL. Measurement of superoxide-derived free radicals in the reperfused heart. J Biol Chem 1988;263:1353–7.
7. Marubayashi S, Dohi K, Ezaki H, et al. Preservation of ischemic liver cell—prevention of damage by coenzyme Q_{10}. Trans Proc 1983;15:1297–9.
8. Paller MS, Hoidal JR, Ferris TF. Oxygen free radicals in ischemic acute renal failure in the rat. J Clin Invest 1984;74: 1156–64.
9. Sanfey H, Buckley GB, Cameron JL. The pathogenesis of pancreatitis: the source and role of oxygen-derived free radicals in three different experimental models. Ann Surg 1985;201:633–9.
10. Patt A, Harken AH, Burton LK, et al. Xanthine oxidase-derived hydrogen peroxide contributes to ischemia reperfusion-induced edema in gerbil brains. J Clin Invest 1988;81: 1556–62.
11. Granger DN, Rutili G, McCord JM. Superoxide radicals in feline intestinal ischemia. Gastroenterology 1981;81:22–9.
12. Walker PM, Lindsay TF, Labbe R, et al. Salvage of skeletal muscle with free radical scavengers. J Vasc Surg 1987;5: 68–75.
13. Detterbeck FC, Keagy BA, Paull DE, Wilcox BR. Oxygen free radical scavengers decrease reperfusion injury in lung transplantation. Ann Thorac Surg 1990;50:204–10.
14. Alican F, Cayirli M, Isin E, Hardy JD. Surgical technique of one-stage bilateral lung reimplantation in the dog. J Thorac Cardiovasc Surg 1971;61:847–56.
15. McCord JM. Superoxide radical: a likely link between reperfusion injury and inflammation. Adv Free Radic Biol Med 1986;2:325–45.
16. Southorn PA, Powis G. Free radicals in medicine. I. Chemical nature and biologic reactions. Mayo Clin Proc 1988;63:381–9.
17. Southorn PA, Powis G. Free radicals in medicine. II. Involvement in human disease. Mayo Clin Proc 1988;63:390–408.
18. Paull DE, Keagy BA, Kron EJ, Wilcox BR. Reperfusion injury in the lung preserved for 24 hours. Ann Thorac Surg 1989; 47:187–92.
19. Ratych RE, Chuknyiska RS, Buckley GB. The primary localization of free radical generation after anoxia/reoxygenation in isolated endothelial cells. Surgery 1987;102:122–31.
20. Cremier J, Jurmann M, Dammenhayn L, et al. Oxygen free radical scavengers to prevent pulmonary reperfusion injury after heart-lung transplantation. J Heart Transplant 1989;8: 330–5.
21. Bando K, Teramoto S, Tago M, Teraoka H, Seno S, Senoo Y. Successful extended hypothermic cardiopulmonary preservation for heart-lung transplantation. J Thorac Cardiovasc Surg 1989;98:137–46.
22. Bonser RS, Fragomeni LS, Edwards BJ, et al. Allopurinol and deferroxamine improve canine lung preservation. Transplant Proc 1990;22:557–8.
23. Fox RB. Prevention of granulocyte-mediated oxidant lung injury in rats by a hydroxyl radical scavenger, dimethlythiourea. J Clin Invest 1984;741:456–64.
24. Toth KM, Harlan JM, Beehler CJ, et al. Dimethylthiourea prevents hydrogen peroxide and neutrophil mediated damage to lung endothelial cells in vitro and disappears in the process. Free Radic Biol Med 1989;6:457–66.
25. Kennedy TP, Rao NV, Hopkins C, et al. Role of reactive oxygen species in reperfusion injury of the rabbit lung. J Clin Invest 1989;83:1326–35.
26. Bishop MJ, Chi EY, Su M, Cheney FW. Dimethythiourea does not ameliorate reperfusion lung injury in dogs or rabbits. J Appl Physiol 1988;65:2051–6.
27. Paull DE, Keagy BA, Entwistle T, Wilcox BE. Effect of superoxide dismutase and catalase infusion at reflow on cardiopulmonary function after lung ischemia in dogs breathing room air. Curr Surg 1988;45:292–4.
28. Paull DE, Keagy BA, Kron EJ, Wilcox BR. Improved lung preservation using a dimethylthiourea flush. J Surg Res 1989;46:333–8.
29. Fox RB, Harada RN, Tate RM, Repine JE. Prevention of thiourea-induced pulmonary edema by hydroxyl-radical scavengers. J Appl Physiol Respir Environ Exercise Physiol 1983;55:1456–9.

DISCUSSION

DR HARVEY I. PASS (Bethesda, MD): What did the lungs look like histologically comparing control and DMTU? How do you know this effect is not really just a wash-out effect of DMTU from the lung that is having a peripheral effect elsewhere? In other words, my basic question is, if you give the DMTU into animals straight, what sort of hemodynamic consequences do you have?

DR LAMBERT: We have unpublished data that show no hemodynamic difference in animals that were given DMTU and animals that received saline solution but did not undergo transplantation. We performed our study in a blinded fashion with all other factors being controlled. Any improvement was due to DMTU therapy alone. We have not evaluated histology between treatment groups.

DR FREDERICK L. GROVER (San Antonio, TX): I enjoyed your paper very much because of our interest in clinical lung transplantation in San Antonio. Dr Charles Bryan of our Pulmonary Medicine Division and Drs David Cohen and John Calhoon from our Cardiothoracic Surgery Division have been performing very similar experiments comparing Euro-Collins solution with Euro-Collins and glutathione, and also Viaspan, which is a colloid that contains glutathione, allopurinol, and several other ingredients. Glutathione is an intracellular tripeptide that reduces hydrogen peroxide or lipid hydroperoxides to less toxic compounds.

The end-product of free radicals (malondialdehyde) was measured, with the findings that in the control group there was not an increase in the free radicals in either lung. Left lungs were autotransplanted in the experimental groups. In the Euro-Collins group both the right and the transplanted left lung had an increase in free radical activity. When glutathione was added to the Euro-Collins solution, the group very nearly approached the control group in free radical activity, as did the Viospan group. The Euro-Collins–perfused lungs weighed significantly more than the controls, whereas the glutathione and Viospan-perfused lungs were similar to the control group.

I have two questions. One has already been partially answered, I believe, regarding whether you demonstrated that there was free radical activity that was controlled. The second question is, have you looked at the effects of glutathione? As I recall in your data, pulmonary edema as measured by wet-to-dry weights was not as close to controls in your dimethylthiourea group as it was in our glutathione group, which surprised me somewhat because your physiological data looked very good in your experimental group, with improved oxygenation and pathologically better alveolar preservation.

DR LAMBERT: We have not studied the use of glutathione with our model yet. We do have other unpublished studies that have tested other oxygen free radical scavengers.

Our extravascular lung water data did not demonstrate a difference between our groups at any time point. I am not sure why that is, although I think that all transplanted lungs are going to gain water acutely because the lymphatics are disrupted. We kept our dogs as dry as possible. Our left atrial pressures remained less than 10 mm Hg.

Statement on the Use of Animals in Research

The following statement from the American College of Surgeons is also endorsed by The Society of Thoracic Surgeons

The American College of Surgeons supports the responsible use and humane care and treatment of laboratory animals in research, education, and product safety testing. Further, the membership believes that only as many animals as necessary should be used; that any pain or distress animals may experience should be minimized; and that, wherever feasible, alternatives to the use of live animals should be developed and employed.

The American College of Surgeons believes that now and in the foreseeable future it is not possible to completely replace the use of animals and that the study of whole, living organisms is an indispensable element of biomedical research.

Evaluation of Neck Lymph Node Dissection for Thoracic Esophageal Carcinoma

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We studied a series of 150 patients treated for thoracic esophageal carcinoma at our institution. The patients were divided into two matched groups. Group B underwent transthoracic esophagectomy with mediastinal and abdominal lymphadenectomy only; group A also underwent bilateral neck lymph node dissection. The rates of operative mortality and operative complications did not differ significantly between the two groups. The 5-year survival rate was 38.7% overall (48.7% in group A and 33.7% in group B). Group A had a significantly better survival curve than group B. Twenty patients (26.0%) in group A had metastasis in the dissected neck lymph nodes. The 4-year survival rate of these patients was 47.9%. The significantly better survival of group A and the satisfactory prognosis in the patients with positive cervical lymph nodes demonstrates the effectiveness of neck lymph node dissection in radical operation for thoracic esophageal carcinoma.

(Ann Thorac Surg 1991;51:931–5)

The prognostic value of lymph node resection in cancer operations is a topic of frequent argument. Wide lymphadenectomy is often avoided because it usually carries a high risk, especially in the esophageal surgical field. On the other hand, many surgeons adopt lymphadenectomy for cancer operations on the basis, not of a statistical analysis of its prognostic effect, but of their experience and the historical results of operation. Although from 1962 to 1981 we routinely dissected middle and lower mediastinal and abdominal lymph nodes in our radical operation for thoracic esophageal carcinoma, the 5-year survival rate of our patients stayed around 20%. Starting in 1982, we enlarged the area of lymph node dissection to the whole upper mediastinum, based on the results of lymphoscintigrams of the esophagus [1], on which those lymph nodes were most commonly visualized. Simultaneously, we started a trial of neck lymph node dissection for low-risk patients. After convincing ourselves of the safety of the procedure of neck dissection for thoracic esophageal carcinoma, we started this study.

For editorial comment, see page 884.

Material and Methods

A total of 322 patients with thoracic esophageal carcinoma were admitted to our hospital from December 1985 to December 1989, and 251 (78.0%) underwent esophagectomy. Of these patients, 150 who had good surgical status (average age, 62.4 ± 9.6 years) were entered into this study. They were distributed to thoracic surgeons randomly. The senior thoracic surgeons performing the operations were divided into two groups, one group performing our standard radical operation with neck lymph node dissection (patient group A) and the other performing standard radical operation without neck dissection (patient group B). Table 1 lists the background factors of both groups of patients. The preoperative stage of the carcinomas was assessed using the TNM classification proposed by the Union Internationale Contre le Cancer in 1987 [2], on the basis of the patient's records.

Operative Procedure

All 150 patients received esophagectomy through a right thoracotomy and laparotomy. The right thoracotomy was carried out through the fifth intercostal space. The azygos vein and right posterior bronchial artery were ligated and dissected to thoroughly expose the esophagus and lymph nodes. The superior vena cava, innominate artery, right subclavian artery, the pulmonary branch of the right vagus nerve, and the bilateral recurrent laryngeal nerves were carefully exposed and preserved. After esophagectomy and mediastinal lymphadenectomy were accomplished, the patient was moved to an upright position, and pericardiac and celiac lymphadenectomy was carried out through the upper median laparotomy incision. The stomach or colon was prepared for reconstruction.

Group A patients received additional right and left neck lymph node dissection, which was performed through a collar incision cutting across the left sternocleidomastoid muscle and the bilateral sternohyoid and sternothyroid muscles. The other muscles, including the right sternocleidomastoid muscle, and the thyroid gland, large vessels, and nerves were all preserved. The thoracic duct was ligated and dissected along with the lymph nodes. This neck dissection was performed by head and neck surgeons while the abdominal operation was in progress. In

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Table 1. Comparison of Patient Groups

Factors	Group A (n = 77)	Group B (n = 73)	*p* Value
Male/female	71/6	66/7	NS
Average age	60.5 ± 8.9	64.5 ± 10.0	<0.05
Tumor location in esophagus (upper/middle/lower)	7/42/28	6/52/15	NS
Tumor length on radiograph (cm)	5.6 ± 3.2	6.1 ± 3.2	NS
TNM staging			
T			NS
Tis	3	2	
T1	22	24	
T2	21	13	
T3	23	25	
T4	8	9	
N and M			
N0/N1	34/43	27/46	NS
M0/M1	59/18	58/15	NS
Stage			NS
0	3	1	
I	18	15	
IIa	12	9	
IIb	8	7	
III	16	26	
IV	20	15	

NS = not significant.

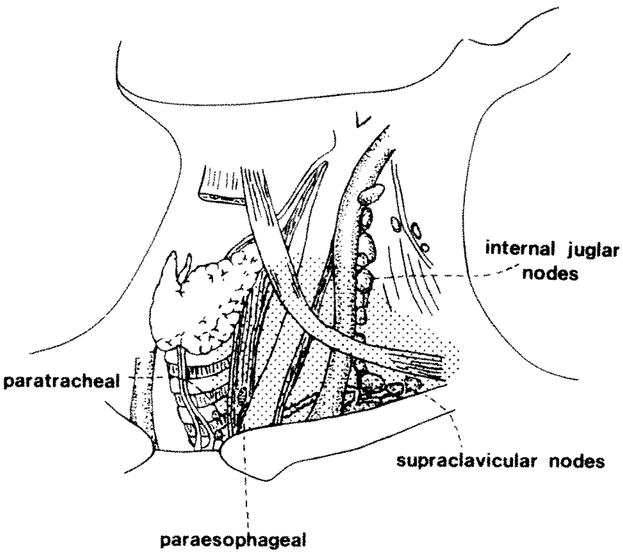

Fig 1. The surgical field in the left neck. The left sternocleidomastoid muscle and the bilateral sternohyoid and sternothyroid muscles were cut. Lymph node dissection in the right neck was performed by pulling up the right sternomastoid muscle. The area of lymph node dissection is shaded.

both groups, the right and left paratracheal, infraaortic arch, infracarinal, periesophageal, right and left paracardiac, perigastric lesser curvature, left gastric, and celiac nodes were resected. The area of lymph node dissection in the neck in group A was tentatively chosen on the grounds of our experience with lymphoscintigraphy and recurrent disease. The bilateral supraclavicular nodes, the lower half of the deep cervical nodes, and the cervical paraesophageal nodes were the targets of neck dissection (Fig 1).

The esophageal reconstruction was pulled up into the neck for anastomosis through the retrosternal route (in the case of stomach) or subcutaneous route (in the case of colon). The stomach was used to reconstruct the esophagus in 66 patients of group A and in 58 patients of group B. The remaining patients had all undergone gastrectomy for ulcer disease or gastric cancer, and in these patients the colon was used.

Postoperative Treatment

Postoperative adjuvant treatments were performed according to another protocol study that was underway. Thirteen patients in group A and 16 in group B received postoperative irradiation, including 5 patients in group A and 9 in group B with residual cancer. Twenty-one patients in group A and 12 in group B received postoperative adjuvant chemotherapy using two doses of intravenous cisplatin (70 mg/m^2) and vindesine (3 mg/m^2). Three in group A and 5 in group B received combined radiotherapy and chemotherapy: irradiation (linear accelerator, x-ray, 50 Gy) for residual cancer, and chemotherapy (cisplatin, 70 mg/m^2, on days 1 and 21; 5-fluorouracil, 700 mg/m^2, on days 1 through 5 and days 21 through 25) as a systemic treatment. Forty patients in each group received no adjuvant treatment.

Differences between the two groups were analyzed statistically by the χ^2 test with the Fisher exact test [3] and *t* test. The survival rates were computed according to the life-table method of Cutler and Ederar [4]; patients who died of operative complications were included. The differences between survival curves were analyzed by the generalized Wilcoxon method [5] and log-rank test [6], censoring operative deaths on the days they occurred.

Results

Except for average age, the patient factors considered, including the TNM stage of the cancer, were not significantly different between the two groups (see Table 1). Five patients in group A and 11 in group B were more than 75 years old. All M1 patients had no distant organ metastasis, but had lymph node swelling in the neck and were diagnosed by ultrasonography or by computed tomographic scan to have metastases (M1; LYM).

The operations lasted an average of 483.0 ± 86.2 minutes in group A and 378.9 ± 79.7 minutes in group B; the difference is significant ($p < 0.01$). The average operative blood loss was 622.5 ± 429.9 mL in group A and 568.2 ± 382.3 mL in group B (not significantly different).

Table 2. Histological Findings of Resected Carcinomas

Finding	Group A	Group B	*p* Value
Longitudinal size (cm)	4.5 ± 2.4	4.9 ± 2.9	NS
No. of patients with/without:			
Lymph node metastasis	49/28	48/25	NS
Neck lymph node metastasis	20/57	. . .	
Average number of:			
Dissected lymph nodes	69.0 ± 6.9	36.4 ± 17.6	<0.01
Positive lymph nodes	3.7 ± 6.8	3.2 ± 4.3	NS
Histological diagnosis			NS
Squamous cell carcinoma	70	68	
Adenosquamous carcinoma	2	2	
Anaplastic carcinoma	0	3	
Carcinosarcoma	4	0	
Malignant melanoma	1	0	
Depth of tumor invasion (pTNM[a])			NS
pT1	22	21	
pT2	15	8	
pT3	32	33	
pT4	8	11	

[a] Pathological TNM classification.

NS = not significant.

Histopathology

Histological findings from the resected specimens are shown in Table 2. The tumors averaged 0.4 cm larger in group B than in group A, but the difference was not statistically significant. Metastasis was found histologically in resected lymph nodes in 97 (64.7%) of the 150 patients. Twenty patients (26.0%) in group A had positive lymph nodes in the neck. Because neck as well as thoracic lymph nodes were resected in group A, a significantly larger average number of lymph nodes was resected in group A patients than in group B patients. An average of 0.5 more lymph nodes were positive for metastasis in group A patients than in group B patients, but this difference is not significant.

Most of the lesions were squamous cell carcinomas (90.9% in group A and 93.2% in group B). No adenocarcinomas were included in this series because the series was limited to patients with thoracic esophageal carcinoma. The histopathological depth of tumor invasion, classified using the pT component of the pTNM classification [2], showed no significant difference between the two groups.

Table 3. Operative Complications by Patient Group

Complication	Group A	Group B	*p* Value
Anastomotic leakage	26 (1[a])	17	NS
Vocal cord paralysis	11 (1[a])	15	NS
Pneumonia	7 (1[a])	12 (6[a])	NS
Anastomotic stricture	8	9	NS
Wound infection	5 (1[a])	9 (1[a])	NS
Empyema	1	5 (1[a])	NS
Hepatic failure	2	5	NS
Renal failure	4	2 (1[a])	NS
Myocardial infarction	1	1	NS
Peritonitis	1	1	NS
Ileus	2	0	NS
Chylothorax	0	3 (1[a])	NS
Cerebral infarction	0	1	NS
Bleeding	1 (1[a])	0	NS
Other	5	1	NS
No complication	29	18	NS

[a] Fatal complication.

NS = not significant.

Short-Term Results

One patient of each group died within 30 days after operation. Another patient in group A and 8 in group B died of operative complications. The operative mortality rate was 7.3% of 150 patients (2.6% in group A and 12.3% in group B); the difference between the two groups is statiscally significant ($p < 0.05$).

The number of patients without surgical complications was 29 (37.7%) in group A and 18 (24.7%) in group B; the difference is not significant. The operative complications are shown in Table 3. One patient in group A died of postoperative *Pseudomonas aeruginosa* pneumonia 4 days after operation. Another patient in group A died of infection of a tracheostomy that was created to relieve aspiration pneumonia, resulting in massive bleeding from the innominate artery. One patient in group B died of empyema caused by an infected chylothorax. Another patient in group B died of renal failure caused by wound infection. The other fatal complications in group B were pneumonias.

The most frequent postoperative complication was an anastomotic leakage. The rate of salivary fistula was higher in group A than in group B, but the rate of recurrent nerve palsy was not, despite the additional neck lymph node dissection in group A. All but 1 of the cases of vocal cord palsy were caused by mediastinal lymph node dissection. Another complication caused by neck lymph node dissection was an accidental recurrent nerve injury in the left neck. The two groups did not differ statistically in the incidence of specific complications.

The average duration of hospital stay, including 3 weeks of preoperative examination and more than 6 weeks of postoperative adjuvant treatments, which start 4 weeks after operation, was 82.0 ± 34.6 days for group A

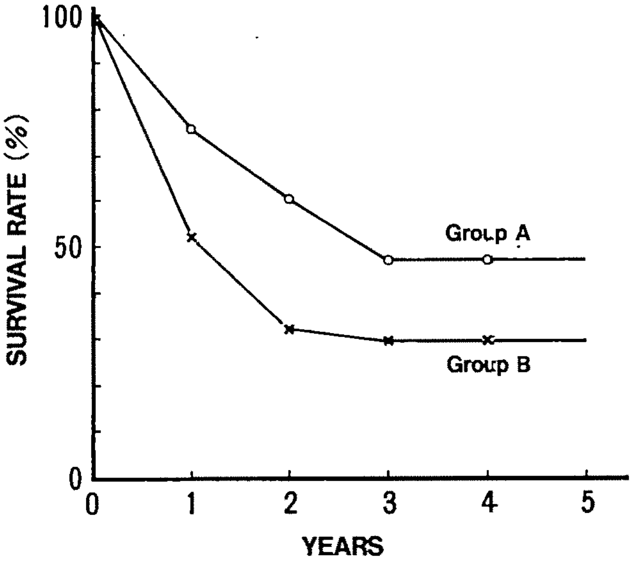

Fig 2. Survival curves for the patients in the two groups, generated using the life-table method. The 3-year and 5-year survival rates were 48.7% and 48.7% in group A and 33.7% and 33.7% in group B, respectively. The difference between these two survival curves was significant ($p < 0.01$).

and 92.8 ± 45.5 days for group B. The difference was not significant. Even patients who had no complications and received no adjuvant treatments stayed in the hospital for at least 2 months.

Long-Term Results

A total of 27 patients in group A and 42 in group B died by December 1989. Thirty-nine patients died of recurrent disease: 18 in group A and 21 in group B. Among them, 16 patients, including 3 who had received neck lymph node dissection, had recurrent disease in the lymph nodes; nine of the recurrences were in the neck. In 6 patients, the first recurrent disease was found in the adjacent organs; in 9, liver; 3, lung; 3, brain; 3, pleura; and 2, other sites. Four patients in each group died of other diseases. The cause of death was unknown in 3 patients of group A and 8 of group B. The differences between the two groups were not significant.

Thirty-four patients in group A and 26 in group B were alive after 3 years. The 5-year survival rate after operation for all 150 patients was 38.7%; 48.7% for group A and 33.7% for group B. Figure 2 shows the postoperative survival curves for the two groups, which differ significantly ($p < 0.01$). Even after patients older than 75 years or patients who died of operative causes are excluded, the two survival curves remain significantly different ($p < 0.05$). The 4-year survival rates for patients who received no adjuvant treatment in group A (40 patients) and in group B (40 patients) were 48.3% and 32.1%, respectively, and the difference between the two survival curves was significant ($p < 0.05$). Though the survival curves for patients who received adjuvant chemotherapy or radiotherapy in group A were also better than those in group B, the difference was not significant.

After stratification by tumor stage, group A showed a better survival curve in stage III ($p < 0.05$) and in stage IV ($p < 0.01$). The 3-year survival rates in group A were as follows: stage 0, 100%; stage I, 45.8%; stage IIa, 81.8%; stage IIb, 71.4%; stage III, 49.9%; and stage IV, 31.0%. In group B, survival in stage 0 was 100%; stage I, 75.0%; stage IIa, 14.7%; stage IIb, 100%; stage III, 27.3%; and stage IV, 0%.

In 20 patients in group A (26.0%), metastasis was found in the resected neck lymph nodes. Eleven of these patients are alive, and 6 of them lived more than 3 years. The 4-year survival rate for these 20 patients was 47.9% (life-table method).

Comment

The primary aim of surgical treatment for cancer is to cure the disease or to prolong life. Some believe that blunt esophagectomy without thoracotomy is safe and is far better tolerated physiologically than the combined transthoracic and abdominal operations [7, 8]. On the other hand, Caracci and associates [9] and Shahian and coworkers [10] demonstrated the superiority of transthoracic esophagectomy over blunt dissection in terms of both morbidity and long-term survival. Tumors in the thoracic esophagus spread to mediastinal as well as to supraclavicular and subdiaphragmatic nodes [11]. Surgical resection of those lymph nodes along with the esophageal lesion seems to improve the prognosis of the patient. We have been resecting mediastinal and abdominal lymph nodes since 1962. After that operation, recurrent disease most often appeared in the neck. At that point, we developed lymphoscintigraphy of the thoracic esophagus, which often visualized the neck lymph nodes. We tried neck lymph node dissection in some patients starting in 1982, to confirm the safety of the procedure and to establish the technique. Then, in December 1984, we commenced the trial reported here to evaluate the effect of neck lymph node dissection.

The prognosis of carcinoma located in the upper thoracic esophagus is said to be particularly poor [11]. Of the 150 lesions reported here, 8.7% were located in the upper thoracic esophagus. The distribution of tumor location in our series was about the same as in the series reported by Akiyama and associates [12], and included larger percentage of carcinoma in the upper thoracic esophagus than the series of Caracci and associates [9]. The Japanese Committee for Registration of Esophageal Carcinoma Cases reported 5,506 esophageal carcinomas resected in Japan [13] including 4,685 thoracic esophageal carcinomas: 390 (8.3%) were located in the upper, 2,957 (63.1%) in the middle, and 1,338 (28.6%) in the lower thoracic esophagus. The distribution of tumor locations in our series is the same as that of average cases resected in Japan.

Our resectability of 78.0% was higher than that reported by Akiyama and colleagues [12] or by Fekete and associates [14]. We included patients who received a palliative operation (17 with T4 disease and 19 with pT4 disease). We prefer a palliative resection to an exploratory thoracotomy or to a bypass operation even in cases in which part of the tumor must be left in the mediastinum, because we expect a better quality of life or because we hope it may be possible to achieve local tumor control by combined resection or by radiation therapy.

The overall operative mortality rate of 7.3% in our series seems satisfactory compared with that of current reports [10, 12, 15, 16]. Our overall 5-year survival rate of 38.7% is as high as those reported by Akiyama and colleagues [12] (34.6%) and Nakayama and co-workers [17] (37.5%).

Though the operation took approximately 100 minutes longer in group A than in group B, neither the average operative blood loss nor the rate of postoperative complications differed significantly between the two groups. The only complication resulting from neck lymph node dissection was one accidental injury of the left recurrent laryngeal nerve. The most frequent complication in both groups was anastomotic leakage. The frequency of anastomotic leakage was higher compared with that of other reported esophageal operations [10, 12, 15]. The surmised reasons were that a high anastomosis in the neck through the retrosternal route caused a poor blood supply in the organ used for reconstruction and that thorough lymph node dissection disturbed the additional blood supply from the covering structure of the anastomosis in group A. In any event, only 1 of 43 anastomotic leaks in our series was fatal. These short-term results show that the burden of neck lymph node dissection for patients with thoracic esophageal carcinoma is acceptable.

The 82 days of hospitalization in group A and 93 days in group B may seem to be exceedingly long. The social situation in Japan allows patients long hospitalization for preoperative examination, and they may stay until they recover completely after operation without financial problems. The average days in our institute were somewhat shorter than at other hospitals in Japan.

The 26% of group A patients who had positive nodes in the neck corresponds to 19 patients in group B. In those 19 patients, carcinoma was possibly left in the neck. The remaining carcinoma might be fatal for some of them. Though the 64.7% overall rate of patients with positive lymph nodes in our series is comparable with reported values [12, 18], the postoperative survival rate is better than that of those series. These results suggest the effectiveness of neck lymph node dissection for survival. Moreover, a 47.9% 4-year survival rate for 20 patients with positive neck lymph nodes indicates that the disease of some of these patients still remained to be localized.

After stratification of the patients by stage, the survival curves for patients in stage III and IV in group A were clearly better than group B, which suggests that neck lymph node dissection was effective for patients in advanced stages.

Although our two groups of patients were operated on by two different groups of surgeons, the surgeons had been working together in the same institution, and performed the procedure with comparable skill. The patients were distributed to surgeons randomly. Therefore, the significantly better survival curve for group A, and the 47.9% 4-year survival for patients with positive nodes in the neck, can be taken to demonstrate that the addition of neck lymph node dissection to the radical operation with mediastinal and abdominal lymph node dissection for thoracic esophageal carcinoma improves the prognosis of the patient.

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References

1. Terui S, Kato H, Hirashima T, et al. An evaluation of mediastinal lymphoscintigraphy for carcinoma of the esophagus studied with ^{99m}Tc rhenium sulfur colloid. Eur J Nucl Med 1982;7:99–101.
2. International Union Against Cancer. TNM classification of malignant tumors. Fully revised edition. New York: Springer-Verlag, 1987.
3. Miettinen OS. Comment. J Am Stat Assoc 1974;69:380–2.
4. Cutler SJ, Ederar F. Maximum utilization of the life table method in analyzing survival. J Chronic Dis 1958;8:699–712.
5. Gehan EA. A generalized Wilcoxon test for comparing arbitrarily singly-censored samples. Biometrica 1965;52:203–24.
6. Peto R, Pike MC, Armitage NE, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. Br J Cancer 1977;35:1–39.
7. Orringer MB, Sloan H. Esophagectomy without thoracotomy. J Thorac Cardiovasc Surg 1978;76:643–54.
8. Steiger Z, Wilson RF. Comparison of the results of esophagectomy with and without thoracotomy. Surg Gynecol Obstet 1981;153:653–6.
9. Caracci B, Garvin P, Kaminski DL. Surgical therapy of advanced esophageal cancer: a critical appraisal. Am J Surg 1983;146:704–7.
10. Shahian DM, Neptune WB, Ellis FH. Transthoracic versus extrathoracic esophagectomy: mortality, morbidity, and long-term survival. Ann Thorac Surg 1986;41:237–46.
11. Sanderson DR, Bernatz PE. Malignant tumors of the esophagus and cardia of the stomach. In: Payne WS, Olsen AM, eds. The esophagus. Philadelphia: Lea & Febiger, 1974:239.
12. Akiyama H, Tsurumaru M, Kawamura T, et al. Principles of surgical treatment for carcinoma of the esophagus: analysis of lymph node involvement. Ann Surg 1981;194:438–46.
13. Japanese Committee for Registration of Esophageal Carcinoma Cases (Chairman; Iizuka T). Parameters linked to ten-year survival in Japan of resected esophageal carcinoma. Chest 1989;98:1005–11.
14. Fekete F, Gayet B, Langonnet F, Lemee J. Radicality in esophageal cancer surgery. Ital J Surg Sci 1987;17:15–20.
15. McKeown KC. Resection of midesophageal carcinoma with esophagogastric anastomosis. World J Surg 1981;5:517–25.
16. Postlethwait RW. Complications and death after operation for esophageal carcinoma. J Thorac Cardiovasc Surg 1983;85:827–31.
17. Nakayama K, Kinoshita Y. Cancer of the gastrointestinal tract: II. Esophagus: treatment—localized and advanced: surgical treatment combined with preoperative concentrated irradiation. JAMA 1974;227:178–81.
18. Jacson JW, Cooper DKC, Guvendik L, et al. The surgical management of tumors of the oesophagus and cardia: a review of the results in 292 patients treated over 15-year period (1961–75). Br J Surg 1979;66:98–104.

Aprotinin Reduces Intraoperative and Postoperative Blood Loss in Membrane Oxygenator Cardiopulmonary Bypass

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To determine whether aprotinin can provide a significant improvement of hemostasis in cardiopulmonary bypass using a membrane oxygenator, we tested this drug in a prospective, randomized, double-blind, placebo-controlled clinical trial. The subjects were 80 male patients undergoing cardiopulmonary bypass for coronary artery bypass grafting. Forty patients received aprotinin and 40 patients served as placebo controls. Aprotinin (4×10^6 KIU) was given as a continuous infusion, starting before operation and continuing until after cardiopulmonary bypass; additionally, 2×10^6 KIU aprotinin was added to the pump prime. Intraoperative and postoperative bleeding, respectively two thirds and one third of the total perioperative blood loss, were both significantly reduced in the aprotinin-treated group ($p < 0.01$). The total average perioperative blood loss, corrected to a hemoglobin concentration of 7 mmol/L, was 550 mL in the aprotinin-treated patients versus 900 mL in the control patients. This reduction in blood loss, furthermore, significantly decreased the amount of postoperative blood transfusions ($p < 0.05$) and increased the percentage of patients who did not receive postoperative donor blood from 42% to 68%. Aprotinin increased the activated clotting time significantly during cardiopulmonary bypass, which led to a reduction in heparin usage. The improved hemostasis during operation, despite the prolonged activated clotting time, might even abolish the need for heparin conversion with protamine at the end of cardiopulmonary bypass, thus allowing retransfusion through cardiotomy suction to be continued, which saves the blood that is currently lost with vacuum suction.

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Intensive contact of blood with the cardiopulmonary bypass (CPB) circuit causes platelet damage and impairment of normal hemostasis [1]. Improvements made in the design of the various parts of the CPB equipment, and particularly the introduction of membrane oxygenators, have contributed to reduce platelet damage. Membrane oxygenators currently do not reduce platelet number or adenosine diphosphate-induced platelet aggregation during CPB [2]. Platelets are, however, still activated, and their function is affected during CPB as shown by the release of β-thromboglobulin from platelets and the prolonged postoperative bleeding times [3]. To protect platelets from activation during CPB, platelet inhibitors such as prostaglandin E_1 [4], prostacyclin [5, 6], and iloprost (ZK 36374) [7] have been used. The major drawback of all these drugs was their strong vasodilating side effect, which prevented the use of sufficiently high dosages to effectively inhibit platelet activation during CPB.

Aprotinin, a proteinase inhibitor, effectively inhibits fibrinolysis [8] and improves perioperative hemostasis in bubble oxygenator perfusion [9]. This study evaluates whether aprotinin treatment will also result in improved perioperative hemostasis with less of an effect on platelets in membrane oxygenator perfusion. We specifically quantified intraoperative blood loss because we observed in our previous study [10] that aprotinin provided improved intraoperative hemostasis during full heparinization.

Material and Methods

Signed informed consent was obtained from all 80 participating, otherwise healthy, male patients scheduled for elective coronary artery bypass grafting. The study protocol was reviewed and approved by the ethical committee of the Onze Lieve Vrouwe Gasthuis.

Patient Exclusion Criteria

The following exclusion criteria were used: a history of allergy, acute pancreatitis and possible previous exposure to aprotinin, thromboembolic disease that required treatment with anticoagulant therapy, severe kidney and liver function disturbances as reflected in an elevated serum creatinine level (>100 mmol/L), and elevated prothrombin time. Patients who were preoperatively treated with acetylsalicylic acid or dipyridamole were excluded from the study.

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Study Drug Administration

Aprotinin (Trasylol) and placebo solution were supplied by Bayer AG (Leverkusen, Germany) in bottles containing 50 mL of saline solution without any other additives or preservatives. Each milliliter of aprotinin solution contained 10,000 kallikrein inactivator units (KIU). The randomization code was only known to the pharmacy of the hospital. We collected the coded vials containing either placebo or aprotinin from the hospital pharmacy in the morning before the operation. We started the infusion of placebo or aprotinin with a bolus of 200 mL (2×10^6 KIU) just after the Swan-Ganz catheter was introduced; thereafter we kept the infusion rate at 50 mL (0.5×10^6 KIU) per hour with an infusion pump (IVAC, San Diego, CA). The total amount of aprotinin delivered by infusion was 4×10^6 KIU before and during bypass.

Cardiopulmonary Bypass

The extracorporeal circuit contained either a William-Harvey membrane oxygenator (model HF-4000, Bard Cardiosurgery Division, Tustin, CA) or a Sci-Med 2 spiral coil membrane oxygenator (model SM 25/system; Sci-med Live Systems Inc, Minneapolis, MN). Both types of oxygenators were randomly used in the two study groups. Polyvinyl chloride tubing was used throughout the extracorporeal circuit, except for the pump tubing, which was made of silicone rubber. The prime of the extracorporeal circuit consisted of 1.5 L Haemacell (Hoechst Holland N.V., Amsterdam, the Netherlands) and 1.0 L Hartmann solution containing 5,000 IU heparin (Leo, Emmen, the Netherlands). To this priming solution we added either saline solution (placebo) or aprotinin (2×10^6 KIU). Heparin (300 IU/kg) was given intravenously before cannulation of the ascending aorta and the right atrial appendage. During CPB we repeated heparin administration (100 IU/kg; intravenous) whenever the activated clotting time (ACT) was shorter than 400 seconds. After CPB the starting dose of heparin was neutralized with protamine sulfate on a 1:1 ratio. The perfusion flow rate during moderate hypothermia was 2.5 $L/m^2 \cdot min$.

During suturing of the distal coronary anastomoses, the aorta was clamped and cardioplegia was achieved with an ice-cold isotonic solution containing 15 mmol K^+, 15 mmol Mg^{2+}, and 1.5 g albumin per liter. Cardioplegia was repeated every 30 minutes. An average of 1.5 L of cardioplegic solution was used and returned to the circulation.

Anesthesia

Premedication was given with lorazepam (Temesta; Wyeth, Hoofddorp, the Netherlands), 4 to 5 mg, 2 hours before induction of anesthesia. Anesthesia was induced with a bolus of alfentanil (Rapifen; Janssen, Tilburg, the Netherlands) (50 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and etomidate (Hypnomidate; Janssen) (0.1 mg/kg) followed by pancuronium bromide (Pavulon; Organon, Oss, the Netherlands) (0.1 mg/kg). Anesthesia was maintained with a continuous infusion of 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ etomidate and 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ alfentanil before CPB; during and after CPB the dose was, respectively, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$. When blood pressure increased the alfentanil concentration was changed and a nitroglycerin infusion was started. At termination of CPB inotropic drugs were given if necessary. All patients were ventilated to normocapnia (arterial carbon dioxide tension, 4.5 to 5 kPa) with an air/oxygen mixture (inspired oxygen fraction, 0.5).

Criteria for Transfusion of Banked Donor Blood Products

During the operation red blood cell concentrates were transfused when the hematocrit value decreased to less than 0.20. In the intensive care unit, red blood cell concentrates were used when the hemoglobin concentration decreased to less than 6 mmol/L, corresponding to a hematocrit value of about 0.30.

Hematology

Preoperatively, typically the day before the operation, the bleeding time was determined according to the method of Mielke and associates [11] with a bleeding time testing device (B.T.T. International Medical Products bv, Zutphen, the Netherlands); in addition, the activated prothromboplastin time, prothrombin time, normotest, and thrombotest were determined. These variables were determined again when the patients arrived at the intensive care unit.

During operation, blood samples were taken from the radial artery or arterial line of the extracorporeal circuit 5 minutes before CPB, at 5 and 30 minutes of CPB, at the end of CPB, and 30 minutes after protamine sulfate administration.

Cell Counts

Two milliliters of blood containing 0.01 mol/L ethylenediaminetetraacetic acid was collected for platelet counts using a fully automated hematology analyzer (E 5000, Toa Medical Electronics Co, Kobe, Japan).

Activated Clotting Time

Two milliliters of blood was collected in a glass vacuum tube containing 12 mg of diatomaceous earth for determination of the ACT. All ACTs were measured with a Hemochron 400 automated timing system (International Technidyne Corp, Edison, NJ). Activated clotting times exceeding 1,000 seconds were interrupted.

β-Thromboglobulin

β-Thromboglobulin concentrations were determined by means of a radioimmunoassay (Amersham, Amersham, UK). Samples were collected in chilled tubes containing platelet inhibitors (Amersham).

Determination of Perioperative Bleeding

During operation, particularly at the end of CPB, the surgeon and the first assistant scored the "dryness" of the operative field on a scale ranging from 1 to 5. A score of 1 was associated with a "bone dry" operative field, whereas a score of 5 was associated with a "very wet" operative field. To assess blood loss during the operation, all used

Table 1. Characteristics of the Study Population

Characteristic	Aprotinin	Placebo
Angina (NYHA class)	2.70 ± 0.13	2.97 ± 0.10
Age (y)	57.6 ± 1.40	57.0 ± 1.39
BSA (m^2)	1.97 ± 0.02	1.91 ± 0.02
Preop Hb (mmol/L)	92 ± 5	93 ± 6
CPB time (min)	108 ± 6.10	104 ± 5.14
Cross-clamp time (min)	64 ± 4.16	62 ± 3.17
Cardioplegia (mL)	1380 ± 57	1671 ± 341
Urine output (mL)	1523 ± 122	1654 ± 100
Infusion fluids (mL)	3517 ± 187	3215 ± 168

BSA = body surface area; CPB = cardiopulmonary bypass; Hb = hemoglobin; NYHA = New York Heart Association.

Table 2. Dryness of the Operative Field[a]

Measurement	Aprotinin	Placebo	*p* Value
Surgeon	2.17 ± 0.11	2.94 ± 0.15	<0.05
First assistant	2.20 ± 0.16	3.18 ± 0.14	<0.05
Closing time (min)	36.90 ± 1.91	42.80 ± 2.7	NS

[a] Possible score ranging from 1 to 5: 1 = "bone dry," 5 = "very wet."
NS = not significant.

gauzes were weighed and washed in water to achieve lysis of the red blood cells; thereafter the hemoglobin concentration of the washing fluid was measured. In addition, the volume and hemoglobin concentration of the fluid in the vacuum suction canisters were measured. This blood loss was expressed in milliliters of blood with a hemoglobin concentration of 7 mmol/L.

After operation we checked the volume of the shed mediastinal blood loss collected in the Pleur-Evac (Code no: A-4000; Howmedica, International, Dublin, Republic of Ireland) hourly. The Pleur-Evac was removed on the first postoperative day. The contents of the Pleur-Evac were anticoagulated with 5 mL of 0.4 mol/L ethylenediaminetetraacetic acid so that we could measure the total hemoglobin concentration. Again, we expressed this blood loss in milliliters with a hemoglobin concentration of 7 mmol/L.

Statistics

All values are expressed as mean ± standard error of the mean. Statistical analysis was done with a nonparametric statistical test for independent samples, in this case the Mann-Whitney test. A *p* value smaller than 0.05 was considered significant.

Results

There were no significant differences in patient population, cardiopulmonary bypass duration, aortic clamp time, volume of cardioplegic solution, intraoperative urine output, and volume of infusion fluids (Table 1).

We did not observe any adverse effect during or after operation that could be related to the use of aprotinin. Patients from both groups invariably did well after operation. There were no electrocardiographic or enzymatic indications of perioperative myocardial infarction; furthermore, there was no difference between the two groups in postoperative hemodynamics or duration of intensive care treatment and total hospitalization.

Dryness of the Operative Field

The "dryness score" issued by the first assistant and surgeon showed a significantly dryer operative field in the aprotinin-treated patients (Table 2). This subjective difference in dryness resulted in a shorter so-called closing time, ie, the time interval between the end of extracorporeal circulation and the end of skin closure. In the aprotinin-treated group the closing time was about 6 minutes, 14% shorter than in the placebo group, although this difference in closing time was not significant.

Blood Loss

The intraoperative blood loss accounted for two thirds, the postoperative blood loss for one third of the total perioperative blood loss (Table 3). Intraoperative blood loss was significantly reduced in the aprotinin-treated patients by an equivalent of about 200 mL of blood.

Aprotinin-treated patients also had significantly reduced mediastinal drainage production, particularly in the first 8 postoperative hours (Table 4). Based on the hemoglobin concentration of the fluid in the Pleur-Evac, which was 1.9 ± 0.2 mmol/L in the aprotinin group and 2.6 ± 0.18 mmol/L in the control group, we calculated a significantly reduced postoperative blood loss (7 mmol/L) of 126 ± 10 mL in the aprotinin group versus 250 ± 20 mL in the placebo group in the first 18 hours.

Banked Donor Blood Products

During operation both the control and aprotinin patients needed similar amounts of banked donor blood products. After operation, aprotinin-treated patients needed significantly less banked donor blood products. Also, the percentage of patients that received banked donor blood products was reduced by 26% (Table 5).

Hematology

After heparinization the ACT increased from 150 to 495 ± 29 seconds in the untreated patients; it was significantly

Table 3. Blood Loss[a]

Measurement	Aprotinin	Placebo	*p* Value
Intraoperative			
Gauzes	203 ± 108	284 ± 159	<0.02
Suction	217 ± 144	363 ± 247	<0.02
Total intraoperative	420 ± 173	647 ± 231	<0.01
Postoperative	139 ± 91	264 ± 139	<0.01
Total perioperative	559 ± 109	911 ± 170	<0.01

[a] Values are given in milliliters of blood with a hemoglobin concentration of 7 mmol/L.

Table 4. Shed Mediastinal Blood[a]

Postoperative Hour	Aprotinin	Placebo	p Value
1	69 ± 9	96 ± 17	NS
2	35 ± 4	76 ± 9	<0.02
3	28 ± 4	53 ± 5	<0.01
4	27 ± 6	42 ± 4	<0.05
5	22 ± 2	31 ± 3	NS
6	14 ± 1	25 ± 3	<0.05
7	14 ± 2	26 ± 4	<0.05
8	12 ± 2	21 ± 3	<0.05
Total volume	221	370	

[a] All values are in milliliters.

NS = not significant.

higher, 834 ± 30 seconds, in the aprotinin-treated patients ($p < 0.001$). Throughout CPB the ACT of the aprotinin-treated patients remained significantly higher than the ACT of the untreated patients (Fig 1). Additionally, in contrast to patients receiving placebo, aprotinin-treated patients did not receive extra heparin during bypass to keep the ACT greater than 400 seconds. The ACTs of both groups returned to normal after protamine administration.

β-Thromboglobulin

β-Thromboglobulin concentrations increased similarly in both groups of patients throughout CPB. At the end of CPB a threefold increase of β-thromboglobulin was measured (Fig 2).

The bleeding time increased in both groups as a result of CPB. This increase in bleeding time was not significantly different between the groups, mainly because of the large interindividual spread of preoperative bleeding times. The activated prothromboplastin time, prothrombin time, and platelet and leukocyte counts on the first postoperative day did not differ significantly between groups (Table 6).

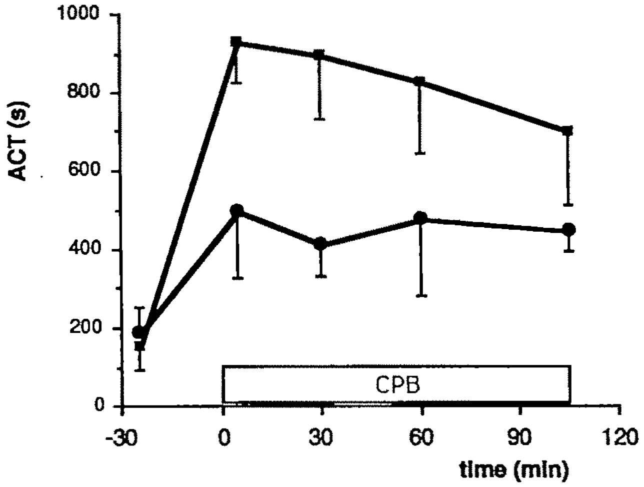

Fig 1. The activated clotting time (ACT) was significantly higher after administration of heparin in the patients treated with aprotinin (squares) than in the control patients (circles). (p < 0.01 during the whole procedure of cardiopulmonary bypass [CPB].)

Comment

Our results clearly show that aprotinin treatment in CPB with membrane oxygenator perfusion significantly reduces both intraoperative and postoperative blood loss, which eliminates the need for postoperative blood transfusions in 68.5% of the treated patients.

Table 5. Usage of Banked Donor Blood Products

Blood Product	Aprotinin	Placebo	p Value
Intraoperative			
Packed cells (units)	1.5 ± 0.2	1.6 ± 0.2	NS
FFP (units)	0.2 ± 0.09	0.2 ± 0.14	NS
Patients no blood (%)	25.70	28.50	
Postoperative			
Packed cells (units)	0.4 ± 0.11	0.9 ± 0.16	<0.05
FFP (units)	0.3 ± 0.13	1.0 ± 0.20	<0.05
Patients no blood (%)	68.50	42.80	

FFP = fresh frozen plasma; NS = not significant.

This study also shows that the bulk of perioperative blood loss occurs intraoperatively. We found that intraoperative blood loss accounts for two thirds and postoperative blood loss for only one third of the total blood loss.

The effect of aprotinin treatment on the reduction of intraoperative blood loss was clearly noticed by the surgeons, because they operated in a remarkably dry operative field right from the start of operation [12]. We could substantiate this subjective indication of improved intraoperative hemostasis because aprotinin treatment resulted in saving an equivalent of 200 mL of blood during operation. This improvement in intraoperative hemosta-

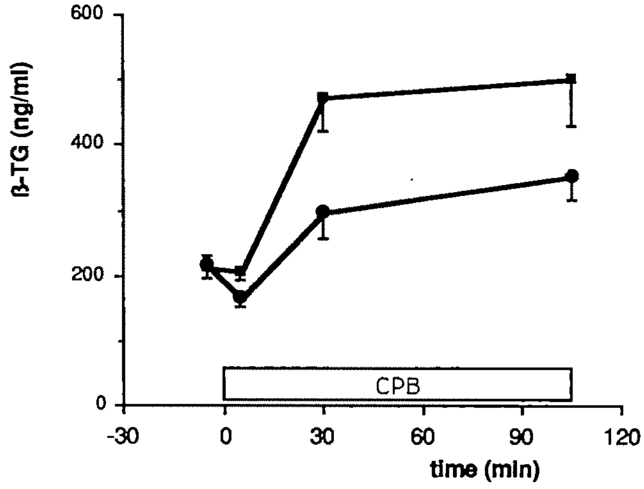

Fig 2. β-Thromboglobulin (β-TG) concentrations increased in both aprotinin-treated (squares) and control patients (circles) during cardiopulmonary bypass (CPB). No significant differences were observed between the two groups.

Table 6. Postoperative Coagulation Variables[a]

Variable	Aprotinin	Placebo
Bleeding time (s)	410 ± 29	459 ± 36
Hb (mmol/L)	6.8 ± 0.20	6.4 ± 0.10
APTT (s)	47 ± 2.00	43 ± 1.40
PTT (s)	15 ± 0.20	16 ± 0.30
Platelets		
Preop	236 ± 16.0	242 ± 16.8
Postop	141 ± 7.3	138 ± 7.9

[a] There were no significant differences between the aprotinin and placebo groups.

APTT = activated partial thromboplastin time; Hb = hemoglobin; PTT = prothrombin time.

sis despite full heparinization is most likely associated with a preservation of the hemostatic function of platelets. We previously demonstrated in control patients a 50% loss of the adhesive receptor from the platelet membrane (GP1b) within the first 5 minutes of CPB. In aprotinin-treated patients, however, we found full preservation of this adhesive receptor throughout CPB [13]. The adhesive receptor on the platelet membrane plays an important role, independent of clotting factors, in the initial platelet plug formation on damaged vascular endothelium. The preservation of this receptor by aprotinin treatment most likely explains the improved intraoperative hemostasis despite heparinization. In contrast, the α-granule release from platelets, demonstrated by β-thromboglobulin, was not protected by aprotinin. This indicates that the platelets can still be activated by various agonists, such as ADP.

The significantly reduced intraoperative blood loss with aprotinin treatment was not sufficient to result in a significant reduction of intraoperative packed cell usage. A large percentage of patients (75%) in both groups still needed packed cells to correct for a low hematocrit value during bypass. This low hematocrit value is mainly a result of both clear prime and the large circulating volume caused by nitroglycerin infusion, which was used routinely in all patients. It is clear that further reduction of intraoperative packed cell usage has to be obtained by adaptation of the anesthesia protocol with respect to the afterload reduction and by defining the lowest acceptable hematocrit values during and shortly after bypass. In this regard a hematocrit value of 0.28 shortly after bypass is probably sufficient [14].

Another important intraoperative observation was that the vacuum suction, started after the administration of protamine, accounted for 54% of the total intraoperative blood loss. Because the hemostasis was well maintained independent of full heparinization and anticoagulation, as witnessed by the prolonged ACT values during bypass, the use of protamine to neutralize the heparin could be abandoned and continuation of retransfusion of cardiotomy suction remained possible. Not only can this double the efficacy of saving blood intraoperatively, but it can also avoid the well-documented negative effects of protamine on platelet function [1] and on the cardiovascular system [15].

In general, interventions seeking to reduce blood loss and, consequently, donor blood requirements will profit most by measures that reduce intraoperative blood loss because two thirds of the total blood loss occurs intraoperatively.

In the postoperative period the reduction in shed mediastinal blood and donor blood requirements in the aprotinin group correlated nicely; both were approximately halved. Postoperatively donor blood was needed in 32% of the aprotinin-treated patients, whereas 57% of the placebo-treated patients needed donor blood. The routine hemostasis variables that we measured on arrival in the intensive care unit were similar in both groups and did not explain the improved postoperative hemostasis in the aprotinin-treated group. In particular, platelet numbers did not differ in both groups and bleeding times were not significantly different, although they tended to be somewhat higher in the placebo group. With an improvement of platelet hemostatic function in the aprotinin group, as previously indicated by a preservation of the platelet adhesive receptors [13], one may expect an improved bleeding time postoperatively. Indeed, an improved postoperative bleeding time with the use of aprotinin was measured in earlier studies using bubble oxygenators [9]. To explain this discrepancy with our current findings one has to bear in mind that platelet function during membrane oxygenator perfusion is less impaired than during bubble oxygenator perfusion, and therefore the additional favorable effect of aprotinin on platelet function during CPB could fall within the outer limits of the sensitivity of the bleeding time determination. Electrocardiography was routinely performed in the postoperative period. Because no indications of infarctions were observed, further biochemical measurements (creatine kinase-MB) were not performed.

In conclusion, aprotinin treatment reduces intraoperative and postoperative blood loss significantly even in membrane oxygenator perfusion, which maintains better platelet function, resulting in a decrease of postoperative donor blood requirements by about half. In addition, the need for postoperative blood transfusions in patients after CPB was reduced from 57% to 32%. Because the bulk of perioperative blood loss is caused by intraoperative bleeding, further efforts to reduce donor blood requirements should be concentrated particularly on reduction of intraoperative blood loss.

References

1. Mannen FM, Koets MH, Washington BC, et al. Hemostasis changes during cardiopulmonary bypass surgery. Semin Thromb Hemost 1985;11:281–92.
2. Harder MP, Leusink JA, de-Nooy EH, Gerding A, Wildevuur ChRH. Haematological characteristics of a new membrane oxygenator: the Cobe CML. J Cardiovasc Surg 1987;28:627–32.
3. Harker LA, Malpass TW, Branson HE, et al. Mechanism of abnormal bleeding in patients undergoing cardiopulmonary

bypass: acquired transient platelet dysfunction associated with selective alpha granule release. Blood 1980;56:824–34.

4. Van den Dungen JJAM, Karliczek GF, Brenken U, Homan van der Heide JN, Wildevuur ChRH. The effect of prostaglandin E_1 in patients undergoing clinical cardiopulmonary bypass. Ann Thorac Surg 1983;35:406–14.
5. Malpass TW, Amory DW, Harker LA, Ivey TD, Williams DB. The effect of prostacyclin infusion on platelet hemostatic function in patients undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg 1984;87:550–5.
6. Fish KJ, Sarnquist FH, van Steenns C, et al. A prospective randomized study of the effects of prostacyclin on platelets and blood loss during coronary bypass operations. J Thorac Cardiovasc Surg 1986;91:436–42.
7. Kappa JR, Horn MK, Fisher CA, et al. Efficacy of iloprost (ZK36374) versus aspirin in preventing heparin-induced platelet activation during cardiac operations. J Thorac Cardiovasc Surg 1987;94:405–13.
8. Fritz H, Wunderer G. Biochemistry and applications of aprotinin, the kallikrein inhibitor from bovine organs. Arzneim Forsch Drug Res 1983;33:479–94.
9. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high-dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
10. Van Oeveren W, Harder MP, Roozendaal KJ, Eijsman L, Wildevuur ChRH. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:788–97.
11. Mielke CH Jr, Kaneshiro MM, Mahler IA, Weiner JM, Rapaport SI. The standardized normal Ivy bleeding time and its prolongation by aspirin. Blood 1969;34:204–15.
12. Alajmo F, Calamai G, Perna AM, et al. High-dose aprotinin: hemostatic effects in open heart operations. Ann Thorac Surg 1989;48:536–9.
13. Van Oeveren W, Eijsman L, Roozendaal KJ, Wildevuur ChRH. Platelet preservation by aprotinin during cardiopulmonary bypass. Lancet 1988;2:644.
14. Cosgrove DM, Loop FO, Lytle BW, et al. Determinants of blood utilization during myocardial revascularization. Ann Thorac Surg 1985;40:380–4.
15. Frater RWM, Oka Y, Hong Y, et al. Protamine-induced circulatory changes. J Thorac Cardiovasc Surg 1984;87:687–92.

Brain Protection During Circulatory Arrest

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Previous nuclear magnetic resonance studies in this laboratory have shown a beneficial biochemical effect of antegrade cerebroplegia (CP-A) during hypothermic circulatory arrest. This study compared CP-A with other methods of cerebral protection during hypothermic circulatory arrest to assess the clinical utility of this technique. Twenty-three sheep were divided into four groups: systemic hypothermia alone (SYST) and systemic hypothermia combined with external cranial cooling (EXTNL), retrograde cerebroplegia (CP-R), or CP-A. Cardiopulmonary bypass was started, and the sheep were cooled to 15°C and subjected to 2 hours of circulatory arrest. Cardiopulmonary bypass was restarted, and the animals were rewarmed and weaned from cardiopulmonary bypass. Serial neurological examinations were performed and hourly scores assigned until the animals were extubated. Postanesthetic neurological scores improved in all groups throughout the 6-hour recovery period except the CP-R group. The improvement over time for these scores was similar for the EXTNL and CP-A groups and significantly better than for the SYST or CP-R groups ($p = 0.004$). The CP-A group had 5 of 7 animals with deficit-free survival despite the similarity in recovery of baseline brainstem function. We conclude that both antegrade infusion of cerebroplegia and external cranial cooling confer distinct cerebroprotective effects after a protracted period of hypothermic circulatory arrest when compared with the other methods studied.

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Deep hypothermic circulatory arrest has been a useful adjunct in cardiovascular surgery since its clinical introduction by Drew and Anderson in 1959 [1]. Risk of neurological injury has been a major limitation of the duration of circulatory arrest despite the protective effect of hypothermia. Cerebral cortical damage occurs regardless of the ischemic time [2, 3], although the generally accepted safe duration of circulatory arrest has been estimated to be 45 to 60 minutes [4, 5]. The clinical sequelae of this ischemic damage become evident when the ischemic interval is longer than 60 minutes [3, 6].

Various techniques have been devised to overcome this disadvantage including selective perfusion of the brachiocephalic vessels [7], surface cooling (external cranial cooling) [8], and deep hypothermia with continuous, low-flow perfusion [9]. Although these modifications are used in many centers, very few data as to their efficacy are available. A previous report from this laboratory demonstrated the salutary effects of intermittent antegrade infusion of an asanguineous, oxygenated crystalloid solution (cerebroplegia) of the brain during hypothermic circulatory arrest [10]. Phosphorus-31 nuclear magnetic resonance spectroscopy was used to demonstrate that cerebral cortical high-energy phosphate stores and intracellular pH were sustained in animals given cerebroplegia during hypothermic circulatory arrest versus those animals subjected to hypothermic circulatory arrest alone.

The purpose of the present study was twofold: first, to test the hypothesis that the nuclear magnetic resonance spectroscopic finding of improved high-energy phosphate concentrations and increased intracellular pH correlates with improved neurological outcome when cerebroplegia was infused during hypothermic circulatory arrest, and second, to assess the effect of antegrade cerebroplegia on postarrest neurological function when compared with other methods of cerebral protection during hypothermic circulatory arrest.

Material and Methods

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Juvenile female sheep weighing 19 to 44 kg were divided into four groups. The systemic hypothermia group (SYST) ($n = 6$) received cardiopulmonary bypass core cooling to 15°C and did not receive cerebroplegia or external cranial cooling during circulatory arrest. The external cranial cooling group (EXTNL) ($n = 5$) underwent surface cooling, in addition to systemic hypothermia, as a method of cerebral protection during circulatory arrest. The antegrade cerebroplegia group (CP-A) ($n = 7$) was core-cooled to 15°C and received cerebroplegic infusions

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through the common carotid arteries. After core-cooling, the retrograde cerebroplegia group (CP-R) (n = 5) received cerebroplegic infusions delivered through the external jugular veins.

Anesthesia was induced with sodium pentobarbital (5 mg/kg intravenously, SYST and CP-A groups), or ketamine sulfate (20 mg/kg intravenously, EXTNL and CP-R groups) and maintained after endotracheal intubation with halothane 1% and 99% oxygen. The lungs were not inflated during cardiopulmonary bypass or circulatory arrest.

Intravenous cefazolin was given before operation. Under sterile techniques, the femoral vessels were exposed and isolated bilaterally. An arterial catheter was placed to measure systemic pressures and a Swan-Ganz catheter was placed through the femoral vein to measure the pulmonary artery pressures. A 16F cannula was placed in the left femoral artery to provide an arterial cannulation site for cardiopulmonary bypass. Venous return to the bypass circuit was achieved using a 24F lighthouse-tip cannula inserted into the right atrium through the right jugular vein.

The animals receiving cerebroplegia had 14-gauge catheters inserted directly into each carotid artery or external jugular vein. These catheters were connected through a Y connector to an infusion set controlled by a roller pump. The animals receiving external cranial cooling had ice bags placed around the skull before the circulation was arrested. Four frontoparietal electroencephalographic leads were placed on the scalp and sutured in place and the electroencephalographic signals were recorded throughout the experiment until the animal was extubated or had died. Temperature was measured with a thermistor (Yellow Springs Instruments) placed in the nasopharynx. A catheter was inserted into the bladder to measure urine output.

Cardiopulmonary Bypass Technique

The circuit consisted of a Bio-Medicus centrifugal pump (model BP80), a 33-μm arterial filter (Bard H-625), and a membrane oxygenator with integral heat exchanger (Terumo, Capiox 4.3 m^2). A cardiotomy reservoir (Johnson and Johnson, model 1351) was placed in parallel with the venous line for volume administration into the circuit. The circuit was primed with 2 L of Ringer's lactate to which 5,000 units of heparin, 100 mg of lidocaine, and 100 mEq of sodium bicarbonate were added. Arterial blood gases were measured with a Radiometer (model ABL 3) blood gas analyzer.

Heparin (3 mg/kg intravenously) was administered and cardiopulmonary bypass instituted with flow rates of 75 to 100 $mL \cdot kg^{-1} \cdot min^{-1}$. The perfusate was cooled to achieve systemic hypothermia. Alpha-stat blood pH regulation was employed during hypothermia. When the nasopharyngeal temperature reached 15°C, bypass was discontinued and the sheep were exsanguinated, affording circulatory arrest for 2 hours. During circulatory arrest, the extracorporeal blood volume was recirculated slowly through the oxygenator to maintain hypothermia, oxygen tension, and pH for reperfusion after arrest.

Once cardiopulmonary bypass was reestablished, the animals were gradually rewarmed to 35° to 37°C and then separated from bypass. Minimal doses of inotropic support, homologous blood products, and crystalloid infusions were used to maintain blood pressure in the immediate postbypass period. Halothane anesthesia was discontinued once the arterial and venous perfusion cannulas were removed and the incisions closed.

Experimental Protocol

Animals receiving cerebroplegia had either the carotid arteries or external jugular veins (CP-A or CP-R) exposed during the cooling phase of CPB. The composition of cerebroplegia was as follows: 2.5% dextrose and 0.45% sodium chloride, 1,000 mL; sodium bicarbonate, 22 mEq; calcium chloride, 5 mg; mannitol, 12.5 mg; lidocaine, 200 mg; nitroglycerine, 0.5 mg. The average oxygen tension was 600 mm Hg; oxygen content, 20 mL/L; and pH, 8.0. The animals in the CP-A group received an initial bolus of 1 L of the cerebroplegic solution in an antegrade manner through the carotid catheters followed by an additional five doses of 200 mL each administered at 20-minute intervals for a total of 2 L. The animals in the CP-R group received a total of 1,000 mL of cerebroplegia delivered continuously through the jugular vein catheters throughout the 2-hour arrest period. In this group, the jugular venous pressure was continuously measured and maintained at less than 15 mm Hg. Nasopharyngeal temperatures were measured throughout the period of circulatory arrest. Upon termination of the cerebroplegic infusion, the catheters were removed and the puncture sites repaired.

Postoperative Management

Once the incisions were closed the animals received serial neurological examinations. Most animals exhibited increased neurological function 30 to 60 minutes after cessation of anesthesia. The animals remained on the ventilator until their blood gases and respiratory efforts were sufficient for successful extubation. The scoring system used was modeled after the Glasgow Coma Scale. The Ovine Coma Scale was designed to assess neurological function and typical postanesthetic behavior of sheep (Table 1). The eye signs, motor responses, and responses to oropharyngeal stimulation were readily reproducible from animal to animal. The examinations were conducted hourly until the animal was extubated, then daily until the animal died or was killed.

The brain was removed through a craniotomy and fixed in formalin for gross and histological study. A pathologist, blinded to study groups, examined each slide to ascertain evidence of anoxic injury. The electroencephalographic recordings from each animal were interpreted by a neurosurgeon, also blinded to the study groups.

Statistical Analysis

All data are expressed as the mean ± the standard error of the mean. Survival data were analyzed using Student's *t* test to make comparisons between groups by Statgraphics statistical software (STSC Inc, Rockville, MD) on a personal computer. Analysis of variance for repeated measures was employed to analyze the differences in postarrest neurological recovery between groups using the Statistical Analysis System (SAS Institute, Inc, Cary, NC).

Results

Nasopharyngeal Temperature

There were no intergroup differences in nasopharyngeal temperature at the outset of circulatory arrest, but the temperature in the CP-A group was 2 to 3 degrees cooler than in the SYST group at 1 and 2 hours of circulatory arrest (Table 2). No other differences in temperatures were found between any of the groups.

Survival

The mean survival for each group is listed in Table 3. All animals alive at 7 days were killed; therefore, the maximum possible survival time was 7 days. Those animals receiving antegrade infusion (CP-A) and external cranial cooling (EXTNL) survived significantly longer than the group receiving systemic hypothermia alone (SYST).

Table 1. Ovine Coma Scale

Test	Potential Score	Maximum Score
Corneal reflex		2
Brisk	2	
Decreased	1	
Absent	0	
Ciliary reflex		2
Brisk	2	
Decreased	1	
Absent	0	
Pupils		1
Reactive	1	
Nonreactive	0	
Eye opening		2
Spontaneous	2	
With stimulus	1	
Absent	0	
Best motor		4
Stands	4	
Pushes up	3	
Nonpurposeful	2	
Reacts to pain	1	
Absent	0	
Respirations		1
Spontaneous	1	
Absent	0	
Swallowing		2
Spontaneous	2	
With stimulus	1	
Absent	0	
Total score		14

Table 2. Nasopharyngeal Temperatures During Circulatory Arrest[a]

Group	Onset of CA	1 Hour of CA	2 Hours of CA
SYST	14.5 ± 0.3	15.4 ± 0.4	16.0 ± 0.3
EXTNL	15.0 ± 0.0	15.1 ± 0.8	14.5 ± 1.7
CP-A	14.7 ± 0.2	13.4 ± 0.7[b]	13.1 ± 0.7[c]
CP-R	15.0 ± 0.0	14.3 ± 0.8	14.4 ± 1.1

[a] Values are expressed as mean ± standard error of the mean. [b] $p < 0.06$ for CP-A versus SYST. [c] $p < 0.01$ for CP-A versus SYST.

CA = circulatory arrest; CP-A = antegrade cerebroplegia; CP-R = retrograde cerebroplegia; EXTNL = external cranial cooling; SYST = systemic hypothermia.

Not every sheep that resumed spontaneous breathing was able to survive 7 postoperative days. Furthermore, those sheep that were severely incapacitated (breathing spontaneously but either comatose, unable to feed, or stationary) from cerebral injury were killed before the seventh postoperative day.

Four of the 6 animals in the SYST group could not be extubated. The 2 remaining animals were extubated, and 1 survived for a week with mild ataxia that improved by the fifth postoperative day. The other animal was killed within 2 days of operation owing to incapacitating neurological deficits.

All 5 sheep in the EXTNL group were extubated but 2 animals were killed within 48 hours because of severe cerebral dysfunction. Three of the 5 sheep in the EXTNL group survived for 7 days; only 1 of those 3 survivors was free of neurological deficits, and the other 2 had severe ataxia.

All 7 sheep in the CP-A group were extubated. Five of the 7 animals survived 7 days without apparent neurological injury. The remaining 2 animals died within 48 hours of operation. One animal died, possibly due to a respiratory arrest, early on the first postoperative day despite postarrest neurological recovery typical of the long-term survivors in this group. The other was killed at the end of the second postoperative day due to severe neurological injury.

Two of the 5 sheep receiving retrograde cerebroplegia (CP-R) could not be extubated. Of the 3 sheep that were extubated in this group, only 1 animal survived until the seventh postoperative day. This animal had a mild ataxic gait. The 2 remaining sheep had more severe neurological injuries. One animal died within 24 hours after operation and the other required euthanasia on the second postoperative day.

Postoperative Neurological Evaluation

The neurological scores for each group are presented as the percentage of a perfect hourly score (observed score/perfect score × 100) and are shown in Figure 1. The residual effects of anesthesia prevented meaningful neurological examinations until 3 hours after the end of circulatory arrest. The antegrade infusion group (CP-A) had a better mean score than the other three groups at 3 hours ($p < 0.05$). There were no differences after the first

Table 3. Survival After Hypothermic Circulatory Arrest[a]

Group	n	Extubate	Killed <48 h	Mean Survival	Survived 1 week
SYST	6	2	1 (neuro)	1.3 ± 2.8	1—mild ataxia
EXTNL	5	5	2 (neuro)	5.4 ± 1.0[b]	3—1 free of deficit
CP-A	7	7	1 (resp arrest), 1 (neuro)	5.35 ± 1.0[b]	5—all free of deficit
CP-R	5	3	2 (neuro)	1.9 ± 1.3	1—mild ataxia

[a] Values are expressed as mean ± standard error of the mean. [b] $p < 0.03$ versus SYST.

CP-A = antegrade cerebroplegia; CP-R = retrograde cerebroplegia; EXTNL = external cranial cooling; neuro = neurological symptoms; resp = respiratory; SYST = systemic hypothermia.

examination in hourly neurological scores between the antegrade group and those animals receiving only surface cooling. The CP-A group had significantly better postarrest neurological scores than either the SYST group at every interval or the CP-R group at every interval excluding the 4-hour examination ($p < 0.05$).

Electroencephalograms

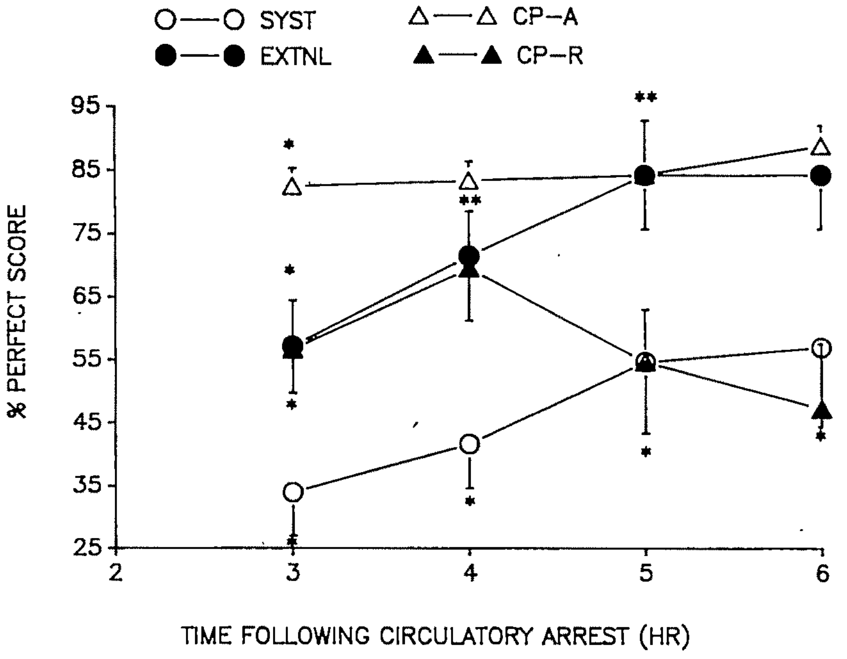
Suitable electroencephalographic recordings were available for 19 of the 23 study animals. The mean time to recovery of signal (return to baseline) in the EXTNL group was 65 ± 17.3 minutes, followed by 98 ± 15.3 minutes in the CP-A group, and 108 ± 45.9 minutes in the SYST group. These differences were not statistically significant. None of the animals in the CP-R group had tracings that returned to baseline. Interestingly, at least 1 of the 7-day survivors in each of the four groups had electroencephalographic traces that never returned to the prearrest baseline.

Postmortem Histology

The brains were fixed in formalin for at least 14 days, after which random sections were obtained from both frontal lobes, the hypothalamus, cerebellum, and occipital lobes. Histological evidence of ischemic cellular injury (neuronal degeneration) was seen in every animal and in every group, regardless of the anatomical region examined, survivorship, or postoperative neurological residua. Hence no differences between the groups were noted.

Comment

Postbypass cerebral injury has compromised otherwise satisfactory results since the inception of open cardiac repair. Evidence of cerebral injury can be demonstrated in a substantial proportion of patients postoperatively, particularly if neuropsychologic testing is done [11]. Focal neurological signs indicative of cerebral injury after circulatory arrest are rare if profound hypothermia is used and the ischemic time does not exceed 1 hour [4, 5]. However, experimental studies have documented cellular damage in animals [12] and humans [13] subjected to cold ischemic times similar to those used clinically. Other studies have shown that IQ scores in children who underwent operative repair of congenital heart defects are less than their age-matched peers without congenital heart disease [14]. Thus, neither cardiopulmonary bypass with moderate hypothermia nor limited circulatory arrest with profound hypothermia offers absolute protection from cerebral cortical damage.



* p < 0.05 vs CP-A ** P < 0.05 EXTNL vs SYST

Fig 1. Neurological score, from the Ovine Coma Scale, after recovery from anesthesia. See text for group abbreviations.

Asanguineous perfusion of the brain during circulatory arrest has been used in previous animal studies with reported benefit. Edmunds and co-workers [15] used Rheomacrodex (10% dextran 40; Pharmacia, Piscataway, NJ) to perfuse the brain during hypothermic circulatory arrest of varying lengths. The animals receiving cerebral perfusion had longer survival and fewer areas of focal necrosis than controls. Wolfson's group performed a series of experiments using hypothermic (0°C) saline cerebral perfusion in dogs [16] and primates [17] subjected to circulatory arrest. These investigators also demonstrated that cold physiological saline perfusion of the brain during circulatory arrest yielded longer postarrest survival than did cold blood perfusion [18]. They also found that trained primates were able to retain previously conditioned responses after cold saline cerebral perfusion during moderate hypothermic circulatory arrest [17]. Using similar techniques, their laboratory studied two groups of animals that received cerebral perfusion with buffered crystalloid during *moderate* hypothermic circulatory arrest. There was complete functional survival in animals with ischemic periods of 90 minutes. The other group was subjected to 2 hours of circulatory arrest. The animals in the group survived without brain injury, but all had gross evidence of spinal cord damage [19]. Mohri and co-workers [4] briefly described their use of asanguineous cerebral perfusion in 5 infants undergoing hypothermic circulatory arrest for repair of congenital heart defects. No adverse neurological sequelae were reported.

Hypothermic reduction of cellular metabolism is not absolute; thus, there are certain obligatory requirements that are not met during circulatory arrest. The rationale for our experiment was to improve cerebral tolerance to extended periods of circulatory arrest using myocardial preservation methodology as a model. Provision of substrate, washout of toxic metabolites, and prevention of early rewarming of the brain before reperfusion were possible by serial infusions of our cerebroplegic solution.

Our findings demonstrate that both antegrade cerebroplegic infusions and external cranial cooling enhanced postarrest recovery of brainstem function to a similar extent. This improvement in neurological function temporally correlates with the recovery of high-energy phosphates demonstrated in our previous study. An attractive hypothesis for the cerebroprotective advantage is that systemic hypothermia combined with cooling the brain directly, rather than systemic hypothermia alone, leads to a rapid and more complete diminution of metabolic activity. Our data show that only the SYST group had significantly higher nasopharyngeal temperatures than the CP-A group. This hypothesis also presumes that provision of oxygen and substrate is unnecessary. When the incidence of postoperative neurological residua is analyzed however, the data suggest that receiving antegrade cerebroplegia is beneficial when compared with external cranial cooling. It is unclear why retrograde infusion of cerebroplegia did not yield a benefit and resulted in a poor outcome. Perhaps diminution of the transcerebral pressure gradient (venous infusion pressure minus arterial hydrostatic pressure) led to accumulation of cerebroplegia in the systemic vasculature raising arterial hydrostatic and intracranial pressure, thus rendering the brain ischemic despite retrograde perfusion.

The electroencephalographic data in this study did not demonstrate a difference between groups. Advances in electroencephalographic technology such as the cerebral function analyzing monitor [20] may yield more accurate, objective, and reproducible information. It also is not surprising that histological evidence of cerebral injury was noted in all four groups. Histological damage was found in all animals subjected to either hypothermic, low-flow cardiopulmonary bypass or hypothermic circulatory arrest in a recent study by Molina and associates [12].

Based on the adverse postoperative neurological residua in the groups not receiving antegrade cerebroplegia, we conclude that during prolonged hypothermic circulatory arrest, infusion of cold, asanguineous, oxygenated crystalloid solution through the carotid arteries affords better brain protection than either external cranial cooling, retrograde infusion of cerebroplegia, or systemic hypothermia alone. Cerebroplegic infusions represent a new method of extending the "safe duration" of hypothermic circulatory arrest. A solution specifically formulated for cerebral protection may produce results that surpass those found in these experiments. Further investigation is necessary in nonhuman species to better assess higher cortical function after circulatory arrest.

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References

1. Drew CE, Anderson IM. Profound hypothermia in cardiac surgery. Report of three cases. Lancet 1959;1:748–50.
2. Folkerth TL, Angell WW, Fosburh RG, Oury JH. Effect of deep hypothermia, limited cardiopulmonary bypass, and total arrest on growing puppies. In: Recent advances in studies in cardiac structure and metabolism; vol 10. Baltimore: University Park, 1975:411.
3. Wells FC, Coghill S, Caplan HL, Lincoln C, Kirklin JW. Duration of circulatory arrest does influence the psychological development of children after cardiac operation in early life. J Thorac Cardiovasc Surg 1983;86:823–31.
4. Mohri H, Barnes RW, Winterscheid LC, Dillard DH, Merendino KA. Challenge of prolonged suspended animation: a method of surface induced deep hypothermia. Ann Surg 1968;168:779–87.
5. Treasure T, Naftel DC, Conger KA, Garcia JH, Kirklin JW, Blackstone EH. The effect of hypothermic circulatory arrest time on cerebral function, morphology, and biochemistry. An experimental study. J Thorac Cardiovasc Surg 1983;96: 761–70.
6. Kramer RS, Sanders AP, Lesage AM, Woodhall B, Sealy WC. The effect of profound hypothermia on preservation of cerebral ATP content during circulatory arrest. J Thorac Cardiovasc Surg 1968;56:699–709.
7. DeBakey ME, Crawford ES, Cooley DA, Morris GC Jr. Successful resection of fusiform aneurysm of aortic arch with replacement by homograft. Surg Gynecol Obstet 1957;105: 656–64.

8. Griepp RB, Stinson EB, Hollingsworth JF, Buehler D. Prosthetic replacement of the aortic arch. J Thorac Cardiovasc Surg 1975;70:1051–63.
9. Kirklin JW, Pacifico AD, Hannah H, Allarde RR. Primary definitive intracardiac operations in infants: intraoperative support techniques. In: Kirklin JW, ed. Advances in cardiovascular surgery. New York: Grune & Stratton, 1973:89.
10. Robbins RC, Balaban RS, Swain JA. Intermittent hypothermic asanguinous cerebral perfusion (cerebroplegia) protects the brain during prolonged circulatory arrest: a phosphorous 31 nuclear magnetic resonance study. J Thorac Cardiovasc Surg 1990;99:878–84.
11. Newman SP. The incidence and nature of neuropsychological morbidity following cardiac surgery. Perfusion 1989;4:93–100.
12. Molina JE, Einzig S, Mastri AR, et al. Brain damage in profound hypothermia. Perfusion versus circulatory arrest. J Thorac Cardiovasc Surg 1984;87:596–604.
13. Muraoka R, Yokota M, Aoshima M, et al. Subclinical changes in brain morphology following cardiac operations as reflected by computed tomographic scans of the brain. J Thorac Cardiovasc Surg 1981;81:364–9.
14. Clarkson PM, MacArthur BA, Barratt-Boyes BG, Whitlock RM, Neutze JM. Developmental progress following cardiac surgery in infancy using profound hypothermia and circulatory arrest. Circulation 1980;62:855–61.
15. Edmunds LH Jr, Folkman J, Snodgress AB, Brown RB. Prevention of brain damage during profound hypothermia and circulatory arrest. Ann Surg 1963;157:637–49.
16. Wolfson SK Jr, Icoz MV, Inouye WY, Parkins WM. Prolonged circulatory arrest with preferential cerebral hypothermia and resuscitation by external cardiac massage. Surg Forum 1964; 15:415–7.
17. Wolfson SK Jr, Icoz MV, Luber S. Preservation of conditioned responses in primates after total circulatory arrest with preferential cerebral hypothermia. Surg Forum 1965;16:409–11.
18. Icoz MV, Wolfson SK Jr. Tolerance to total ischemia in dogs after cold blood or cold physiologic saline perfusion of the brain. Surg Forum 1966;17:403–5.
19. Bacalzo LV Jr, Wolfson SK Jr. Preferential cerebral hypothermia. Tromethamine and dextran 40 and tolerance to circulatory arrest of 90 to 120 minutes. Arch Surg 1971;103:393–7.
20. Nevin M, Colchester ACF, Adams S, Pepper JR. Prediction of neurological damage after cardiopulmonary bypass surgery. Use of the cerebral function analyzing monitor. Anaesthesia 1989;44:725–9.

Bronchogenic Carcinoma With Chest Wall Invasion

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Bronchogenic carcinoma with chest wall involvement continues to present a major clinical challenge. We have treated 52 patients since 1973, excluding those with superior sulcus tumors. There were 37 male and 15 female patients with an average age of 62.9 years. Chest pain was an initial symptom in 37%. All patients had negative mediastinoscopy results. Squamous cell carcinoma was present in 53% and adenocarcinoma in 35%. The median number of ribs resected was two (range, one to six), and only 2 patients required chest wall reconstruction. Pathologic staging was T3 N0 M0 in 83% and T3 N1 M0 in 17%. Operative mortality was 3.8%. Absolute 5-year survival was 26.3%. Patients who had N1 disease had a 5-year survival of only 11%. Radiation therapy was employed in 46% for positive nodes or close margins. Bronchogenic carcinoma with chest wall invasion remains potentially curable if N2 nodes are not involved. The role of radiation therapy has not been clearly defined. Morbidity and mortality should be minimal.

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Bronchogenic carcinoma of the lung remains the leading cause of death due to cancer in the United States. Recently the International Staging System for lung cancer has divided stage III into IIIa and IIIb [1]. Patients who have bronchogenic carcinoma with invasion into the chest wall make up a subset of stage IIIa patients. One of the first reports dealing with this subset of patients was by Grillo and associates [2], who reported on 33 patients with bronchogenic carcinoma that invaded the chest wall. This represented one of the earliest reports of any size to identify bronchogenic carcinoma with chest wall invasion as a curable lesion. The report by Grillo and associates stressed that the tumor was curable by complete resection (full-thickness chest wall was preferable to extrapleural excision), and that chest wall resection as a palliative procedure for pain was not very effective. Since that report others have reported similar conclusions [3–5]. The current report of bronchogenic carcinoma with chest wall invasion updates our experience, reflecting improvements in preoperative staging (eg, mediastinoscopy), the elimination of N2 disease, and improvements in postoperative care. Our findings reinforce those of the earlier report and further emphasize the importance of preoperative staging.

Material and Methods

Our report deals with 52 consecutive patients who underwent resection of bronchogenic carcinoma with chest wall involvement at the Massachusetts General Hospital between July 1973 and September 1988. During this period there were 1,290 patients operated on for bronchogenic carcinoma of the lung. Recurrent carcinomas, metastatic carcinomas, nonbronchogenic cancers, and superior sulcus tumors (Pancoast) were excluded. Minimum follow-up was 17 months. Survival statistics were done by the Kaplan-Meier actuarial method, and survival curves were compared by the log-rank test [6].

Results

Age and Sex

There were 37 men (71%) and 15 women (29%). The average age was 62.9 years (range, 40 to 82 years).

Symptoms

Chest pain was the most common initial symptom and occurred in 37% of the patients. However, in 27% of the patients the initial "symptom" was an incidental finding of a lung lesion on chest roentgenogram. There were 9 patients who had hemoptysis, 5 had a cough, 2 had pneumonia, and 1 had fatigue. Only 2 patients had tenderness over the affected rib on physical examination. All but 3 patients were smokers (97%) with an average of 53 pack-years.

Preoperative Evaluation

The median forced expiratory volume in 1 second was 1.98 (range, 4.04 to 1.10 L) in 39 patients. There was rib destruction noted on the preoperative chest roentgenogram in 10 patients. Percutaneous needle biopsy was done in 26 patients and yielded a positive result in 24 of them. Patients with evidence of distant metastasis were excluded from this study.

Operative Procedure

All patients had bronchoscopy and mediastinoscopy. Patients who had a positive mediastinoscopy did not undergo a thoracotomy. A lobectomy was performed in 25 patients (48%). There were 9 (17%) bilobectomies, 8 (15%) segmentectomies, 6 (12%) pneumonectomies, 2 (4%)

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sleeve lobectomies, and 2 (4%) wedge resections performed. Both sleeve resections were done in patients who had squamous cell carcinoma that was involving the orifice of a major bronchus as well as the chest wall. The median number of ribs resected was two with a range of one to six. Only 2 patients (4%) underwent chest wall reconstruction; both had large anterior chest wall resections. In one the defect measured 10.0 × 9.0 cm in the anterior chest wall, and in the other the defect measured 10.0 × 18.0 cm. Their preoperative 1-second forced expiratory volumes were 1.85 and 2.84 L, respectively. Methyl methacrylate, sandwiched between two layers of Marlex, was used for the reconstruction in both patients as described by McCormack and co-workers [7].

Pathology

Squamous cell carcinoma was present in 28 patients (53%). Adenocarcinoma was present in 18 (35%), adenosquamous in 3 (6%), large cell in 2 (4%) and undifferentiated in 1 (2%). There were no small-cell carcinomas. All lymph nodes were negative in 43 patients, 9 patients had positive N1 nodes, and no patient had positive N2 nodes. N1 nodes were positive in 3 of the 28 patients with squamous cell carcinoma, in 4 of the 18 patients with adenocarcinoma, and in 2 of 2 with adenosquamous carcinoma. The average maximum diameter of the tumor was 5.1 cm. The margins were negative in all patients except 1, in whom the tumor was invasive into the aorta. There were 3 patients in whom the margins were read as "close." These patients had margins of less than 3.0 mm.

Adjuvant Therapy

Nine patients received preoperative radiotherapy (average dose, 37 Gy; range, 30 to 44 Gy). Although there were no strict criteria for administering preoperative radiotherapy, it was given for large tumors or where obtaining an adequate margin would be difficult (eg, costovertebral angle). There were 15 patients who received postoperative therapy (average dose, 37 Gy; range, 8.5 to 55 Gy). All of the 9 patients with positive N1 nodes were given postoperative radiotherapy except 2 patients with marginal pulmonary function (forced expiratory volume in 1 second < 0.8 L). Four other patients received postoperative radiotherapy because their margins were close or positive. The remaining 4 were given postoperative radiotherapy to complement preoperative radiotherapy.

Morbidity and Mortality

There were two in-hospital deaths (3.8%) in this series; however, none within 30 days of operation. One patient died after 56 days as a result of an iatrogenic cerebral vascular accident and 1 of pneumonia 34 days postoperatively. There was a 10% incidence of prolonged air leak (>10 days) that resolved without further surgical intervention. Pneumonia developed in 4 patients. There were two nonfatal pulmonary emboli and one deep venous thrombosis. One patient had a wound cellulitis, and a subscapular fluid collection developed in 1 patient. A transient ulnar neuropathy developed in 1 patient and 1 had atrial fibrillation. There was one postoperative hemorrhage that required reexploration. There were no chest wall motion abnormalities that persisted long term. The median hospital stay was 16 days (range, 7 to 56).

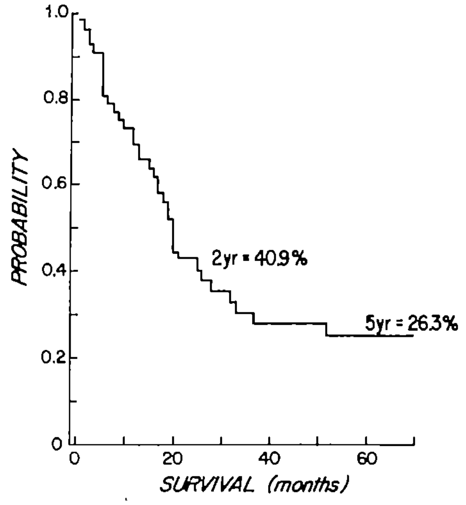

Fig 1. Survival—all patients.

Survival

The overall 2-year survival rate was 40.9%, and at 5 years 26.3% were still alive (Fig 1). The absolute 5-year survival in patients who had negative nodes was 29.1%; it was 11.1% in patients who had positive N1 nodes ($p < 0.05$) (Fig 2). The 5-year survival for patients with squamous cell carcinoma was 25.5%, and for patients with adenocarcinoma the 5-year survival was 30.5% ($p = 0.60$). The patient with a positive margin survived 19 months and had development of a local recurrence at the site of the positive margin. The other 3 patients with close margins (<3.0 mm) survived 8, 12, and 19 months. All of these patients had local recurrence as well. There were no local recurrences in patients in whom the margins were adequate. For those patients who had either preoperative or postoperative radiation therapy, the 5-year survival was only 15.9% as opposed to a 5-year survival of 33.5% for those who did not have radiation therapy ($p = 0.17$). Seven of the 21 patients who received radiation therapy had positive N1 nodes, whereas only 2 of the 31 patients who did not receive radiotherapy had positive nodes.

Comment

The major contribution of the new staging system for lung cancer has been the creation of stage IIIa and IIIb. This has brought to everyone's attention the subset of stage III patients who have a more favorable prognosis. Stage IIIa includes chest wall invasion, superior sulcus tumors, and certain patients with N2 disease. The identification of this favorable IIIa group has made clinicians aware that there is a surgical option for these patients with a reasonable chance for cure. This has been known in the surgical literature for more than 25 years. The report by Grillo and associates [2] from this institution was one of the first series to clarify this favorable group of patients. Our

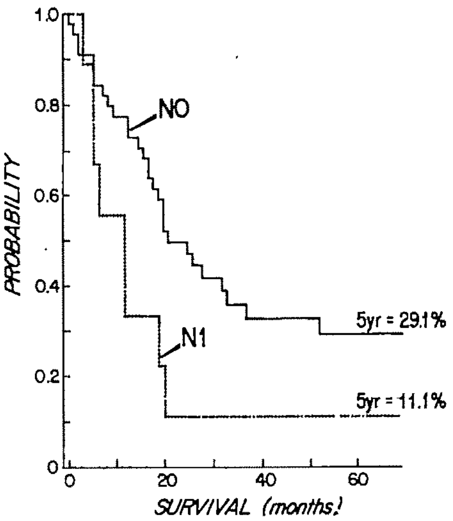

Fig 2. Survival by lymph node involvement.

current report corroborates the previous report and reflects the benefits of improved staging (mediastinoscopy) and postoperative care. It is important to recognize the favorable prognosis of this group of patients because it represents between 4% and 8% of patients with potentially resectable lung cancer [8].

Patients who have carcinoma invading the chest wall often have chest pain as their initial symptom. However, less than half of the patients in this series had chest pain as the sole initial symptom. Plain chest roentgenogram may alert the surgeon that a tumor involves the chest wall if rib destruction is present. Computed tomographic scan is very helpful but not infallible. The recent use of magnetic resonance imaging to determine if there is chest wall involvement is encouraging but awaits further development [9].

Prethoracotomy staging should be performed as completely as possible. The routine use of CBT to evaluate the mediastinum, liver, and adrenal glands has improved the selection of patients for operation. Bone scan and brain computed tomography should also be considered in the preoperative evaluation. Mediastinoscopy is mandatory to rule out patients with N2 disease. The long-term survival in patients with positive mediastinal nodes is very low [3]. Several series in the literature have clearly shown that patients with positive N2 nodes have a poor prognosis (Table 1). Patients who have positive N2 nodes should only be considered for operation as part of a protocol to evaluate other modalities of treatment.

Our 5-year survival rate of 26.3% compares with the survival rate reported with other T3 lesions [16–18]. The survival with no lymph node involvement was 29.1%; with positive N1 nodes, the survival was only 11.1% (1 long-term survivor). We had no patients with positive N2 nodes but few, if any, reported series have had any long-term survivors when N2 nodes are positive (see Table 1).

Our improved mortality rates, as compared with those of others, may reflect recent advances made in preoperative and postoperative care that have occurred since those reports. The advent of the routine use of epidural analgesia, careful postoperative chest physiotherapy, routine use of flexible bronchoscopy, and minitracheostomy have helped reduce postoperative difficulties.

We did not treat any patients for palliation. We believe that chest wall resection for pain relief alone and not for cure should be done only in highly selected patients, if at all. The operation itself is painful and has a substantial morbidity. These risks should be carefully considered before performing a palliative procedure on this type of patient.

Resection of the chest wall should be done as a full-thickness resection and not merely an extrapleural dissec-

Table 1. Survival of Patients With Bronchogenic Cancer With Chest Wall Invasion (Superior Sulcus Tumors Excluded)

Year	First Author	Number of Patients	Long-Term Survival (%)	5-Year Survival by Node Status (%)			Operative Mortality (%)
				N0	N1	N2	
1947	Coleman [10]	5	. . .	. . .	. . .	. . .	20
1966	Grillo [2]	33	19	. . .	. . .	. . .	9
1967	Ramsey [11]	27	10	. . .	. . .	. . .	26
1974	Burnard [12]	68	23	. . .	. . .	. . .	7
1979	Jamieson [13]	43	10	. . .	. . .	. . .	16
1982	Piehler [3]	66	33	54	7	7	15
1982	Patterson [4]	35	38	45	17	0	8.5
1982	Paone [14]	32	35	35	0	0	3.1
1985	van de Wal [8]	12	8	33	0	NP	11
1985	McCaughan [15]	125	40	56	21	21[a]	4
1987	Ricci [5]	77	15	22	12	8	7.8
1991	Allen (present study)	52	26	29	11	NP	3.8

[a] The 21% is the survival for the combined group of N1 and N2 patients.

NP = no patients in this group.

Table 2. Summary of Cell Type

Year	First Author	Percent Squamous	Percent Adenocarcinoma
1991	Allen (present report)	53	35
1985	McCaughan [15]	46	46
1982	Patterson [4]	77	14
1982	Piehler [3]	42	29
1979	Jamieson [13]	65	5
1966	Grillo [2]	75	6

tion. In this series, there were 4 patients who had close margins, and all of them had local recurrence. We recommend the resection of one rib above and one below the lesion and at least a 5.0 cm margin on the tumor. This is also supported by the findings of Piehler, Trastek, and their associates [3, 19]. Trastek and associates [19] reported a 5-year survival of 75% with full-thickness resection and only a 28% 5-year survival when extrapleural resection was done. We believe strongly that resection should be full thickness when the tumor invades the chest wall.

In this series, chest wall reconstruction was performed on only 2 patients. In both of these patients the indication was to cover a large defect in the anterior chest wall. As in other reports, the majority of patients do not require reconstruction [3, 4, 13, 14]. Chest wall reconstruction is not indicated because most of the defects are covered by the scapula and the muscles of the chest. Our indications for reconstruction of the chest wall are in patients with marginal pulmonary reserve to reduce paradox and for cosmetic reasons if the defect is large or located anteriorly. We prefer to use Marlex mesh, either alone or with methyl methacrylate sandwiched between two sheets of Marlex, as described by McCormack and associates [7], for reconstruction.

Squamous cell carcinoma continues to be the predominate cell type in this and other series in which there is chest wall invasion. Our incidence of adenocarcinomas is higher than that reported by Patterson and co-workers [3] or Piehler and colleagues [4] (Table 2). The increase in adenocarcinoma is consistent with more recent reports showing an increase in adenocarcinoma. The difference in survival between squamous and adenocarcinoma was not significant.

The indications for radiotherapy for chest wall invasion remain unclear. The group that received radiotherapy had a lower 5-year survival rate; however, the percentage of patients with N1-positive nodes was much higher in this group of patients. The number of patients was too small to obtain statistically meaningful data in these different groups. Patterson and colleagues [4] did find an improvement in survival with radiotherapy, but it was not significant. The series reported by Paone and associates [14] and by Piehler and co-workers [3] found no difference in long-term survival with the use of radiotherapy. Because the efficacy of radiotherapy is ambiguous, we have tended to administer radiotherapy to patients with large and more aggressive tumors. When the tumor is located in a position that will be difficult to obtain an adequate margin, we administer preoperative radiation therapy. Postoperatively we administer radiation therapy if the margins were close or if there were positive nodes. The true answer to the efficacy of radiotherapy in these types of tumors still awaits a controlled, prospective trial.

References

1. Mountain CF. A new international staging system for lung cancer. Chest 1986;89:225s–32s.
2. Grillo HC, Greenberg JJ, Wilkins EW Jr. Resection of bronchogenic carcinoma involving thoracic wall. J Thorac Cardiovasc Surg 1966;51:417–21.
3. Piehler JM, Pairolero PC, Weiland LH, et al. Bronchogenic carcinoma with chest wall invasion: factors affecting survival following en bloc resection. Ann Thorac Surg 1982;34:684–92.
4. Patterson GA, Ilves R, Ginsberg RJ, Cooper JD, Todd TRJ, Pearson FG. The value of adjuvant radiotherapy in pulmonary and chest wall resection for bronchogenic carcinoma. Ann Thorac Surg 1982;34:692–7.
5. Ricci C, Rendina EA, Venuta F. En bloc resection for T3 bronchogenic carcinoma with chest wall invasion. Eur J Cardio-Thorac Surg 1987;1:23–8.
6. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457.
7. McCormack P, Bains MS, Beattie EJ Jr, Martini N. New trends in skeletal reconstruction after resection of chest wall tumors. Ann Thorac Surg 1981;31:45–52.
8. van de Wal HJCM, Lacquet LK, Jongerius CM. En bloc resection for bronchogenic carcinoma with chest wall invasion. Acta Chir Belg 1985;85:89–94.
9. Haggar AM, Pearlberg JL, Froelich JW, et al. Chest wall invasion by carcinoma of the lung: detection by MR imaging. Am J Roentgenol 1987;148:1075–8.
10. Coleman FP. Primary carcinoma of the lung with invasion of the ribs. Ann Surg 1947;126:156–68.
11. Ramsey HE, Cliffton EE. Chest wall resection for primary carcinoma of the lung. Ann Surg 1968;167:342–51.
12. Burnard RJ, Martini N, Beattie EJ. The value of resection in tumors involving the chest wall. J Thorac Cardiovasc Surg 1974;68:530–5.
13. Jamieson MPG, Walbaum PR, McCormack RJM. Surgical management of bronchial carcinoma invading the chest wall. Thorax 1979;34:612–5.
14. Paone JF, Spees EK, Newton CG, Lillemoe KD, Kieffer RF, Gadacz TR. An appraisal of en bloc resection of peripheral bronchogenic carcinoma involving the thoracic wall. Chest 1982;81:203–7.
15. McCaughan BC, Martini N, Bains MS, McCormack PM. Chest wall invasion in carcinoma of the lung. J Thorac Cardiovasc Surg 1985;89:836–41.
16. Wilkins EW, Scannell JA, Craver JG. Four decades of experience with resections for bronchogenic carcinoma at the Massachusetts General Hospital. J Thorac Cardiovasc Surg 1978;76:364–8.
17. Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. J Thorac Cardiovasc Surg 1988;96:440–7.
18. Landreneau RJ. Carcinoma of the lung. Who will benefit from surgery? Postgrad Med 1990;87:117–35.
19. Trastek VF, Pairolero PC, Piehler JM, et al. En bloc (non-chest wall) resection of bronchogenic carcinoma with parietal fixation. J Thorac Cardiovasc Surg 1984;87:352–8.

Rib Fractures Complicating Median Sternotomy

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The postoperative chest radiographs of 100 consecutive patients undergoing median sternotomy were reviewed for the presence of acute rib fractures. The majority of patients underwent coronary artery bypass grafting. Thirteen patients sustained 15 fractures. Eleven of these fractures were of the left first rib and 7 of the 15 fractures occurred at the costotransverse articulation. The fractures tended to be subtle on the postoperative portable chest radiographs and were initially overlooked in 4 patients. Heavier patients and those with larger body surface areas were more susceptible to the development of fractures. There was no statistical correlation to total operating time, bypass time, or global ischemic time.

(Ann Thorac Surg 1991;51:952–5)

Median sternotomy is now the principal approach for most cardiac operations. Complications involving the sternotomy incision itself are well known [1] and include sternal dehiscence and superficial and deep infections. There have been few reports, however, of rib fractures sustained by this approach [2–5]. This study was undertaken to determine the incidence of rib fractures in patients undergoing median sternotomy and also to ascertain whether identifiable patient features or operative incidents contribute to the development of fractures.

Material and Methods

One hundred consecutive patients undergoing median sternotomy for various cardiovascular operations during the period of August 1, 1988, to August 31, 1989, were entered into the study (Table 1). Eighty-four percent of these procedures were performed or supervised by the same surgeon. The Ankeney retractor was used in all cases with the crossbar positioned caudally and the uppermost blade placed variably between the second and fourth intercostal spaces. The sternal halves were separated as far as necessary for adequate exposure. In addition, if the left internal mammary artery was to be used for bypass grafting, the left half of the sternum was elevated by using a Favaloro retractor.

Pertinent data were collected for each patient by a chart review in which the following characteristics were noted: age, sex, weight, body surface area (m^2), body mass index (weight in kg/[height in m]^2), global ischemic time, cardiopulmonary bypass time, total time in operating room, type of procedure, use of the internal mammary artery, history of previous sternotomy, exploration for postoperative hemorrhage, and 30-day mortality. Postoperative chest radiographs obtained from the time of operation to discharge or death were reviewed independently by two radiologists and any differences were resolved by consensus. The location of a fracture and the postoperative day (POD) on which it was first visualized were noted.

Results

There were 50 men and 50 women in the study group (see Table 1) with a mean age of 58 years (range, 25 to 79 years). Fifteen rib fractures were identified in 13 patients (8 men, 5 women) (Table 2). Twelve patients sustained 1 fracture each, whereas the remaining patient had 3 fractures. There were 12 fractures of the first rib, 11 on the left and 1 on the right. Seven of the fractures were oblique and occurred just beyond the junction (costotransverse articulation) of the neck and the shaft of the ribs (Fig 1) and extended posteriorly toward the tubercle. The eight other fractures were situated in the midshaft (Fig 2).

The fractures were identified prospectively on the radiographs taken on POD 1 except for 4 patients; however, retrospective identification was made in 2 patients. In 1 patient the earliest identification of fracture was on POD 4. The remaining patient is the one with multiple fractures; a left second rib fracture was identified on POD 1, a left first rib fracture on POD 2, and a left third rib fracture on POD 3.

Twelve of the 13 patients had undergone coronary artery bypass grafting, whereas 1 patient had combined mitral valve replacement and coronary artery bypass. In 6 of the 13 patients the left internal mammary artery was used for grafting. Ten of the 100 patients underwent reexploration and 3 of these sustained fractures. Seven patients out of the 100 had prior median sternotomies, and 2 of these 7 sustained rib fractures.

Categorical characteristics listed in Table 3 demonstrate no statistically significant relationship between the various variables and eventual rib fracture. There was no correlation between the occurrence of fractures and the total operating room time, bypass time, cross-clamp time, surgeon, or assistant. The patients in whom fractures occurred were, however, heavier (mean weight, 85 versus 76 kg) and had larger body surface areas (1.93 m^2 versus

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Table 1. Analysis of 100 Patients Undergoing Median Sternotomy

Variable	Percent
Sex	
Male	50
Female	50
Procedure	
CABG	81
Other	19
LIMA	35
Previous sternotomy	7
Reexploration	10
30-day mortality	5
Rib fracture	13

CABG = coronary artery bypass grafting; LIMA = left internal mammary artery.

1.81 m^2) than the rest of the study group (Table 4). Logistic regression analysis with backward elimination was carried out using ten independent variables (age, sex, height, weight, body surface area, body mass index, ischemic time, type of procedure, use of the internal mammary artery, and previous sternotomy). There were no statistically significant predictors by this method, although the closest to significance were previous sternotomy ($p = 0.0808$), height ($p = 0.1435$), body mass index ($p = 0.1534$), and age ($p = 0.1626$).

Comment

To date there have been few reports of rib fractures secondary to median sternotomy [2–5]. Greenwald and associates [5] identified by radionuclide imaging 44 such fractures in 24 consecutive patients, suggesting that the incidence may approach 100%. In the current study fractures were radiographically identified in 13% of the patients, which is within the reported range of 6% to 16% [2, 4]. Bilateral rib fractures do occur [5, 6], and we have encountered such a case outside the study period.

Table 2. Analysis of 13 Patients With Rib Fractures

Patient No.	Age (y)	Sex	Operative Procedure	Ribs Fractured	Postop Day Visible	LIMA
1	65	M	CABG	L1,2,3	2,1,3	Y
2	66	M	CABG, MVR	L1	2	N
3	58	F	CABG	L1	1	N
4	55	M	CABG	R2	1	N
5	64	M	CABG	L1	1	Y
6	72	M	CABG	L1	1	Y
7	67	F	CABG	L1	1	N
8	64	F	CABG	L1	1	Y
9	66	M	CABG	L1	1	Y
10	79	F	CABG	R1	4	N
11	48	F	CABG	L1	1	Y
12	50	M	CABG	L1	1	N
13	74	M	CABG	L1	3	N

CABG = coronary artery bypass grafting; L = left; LIMA = left internal mammary artery; MVR = mitral valve replacement; R = right.

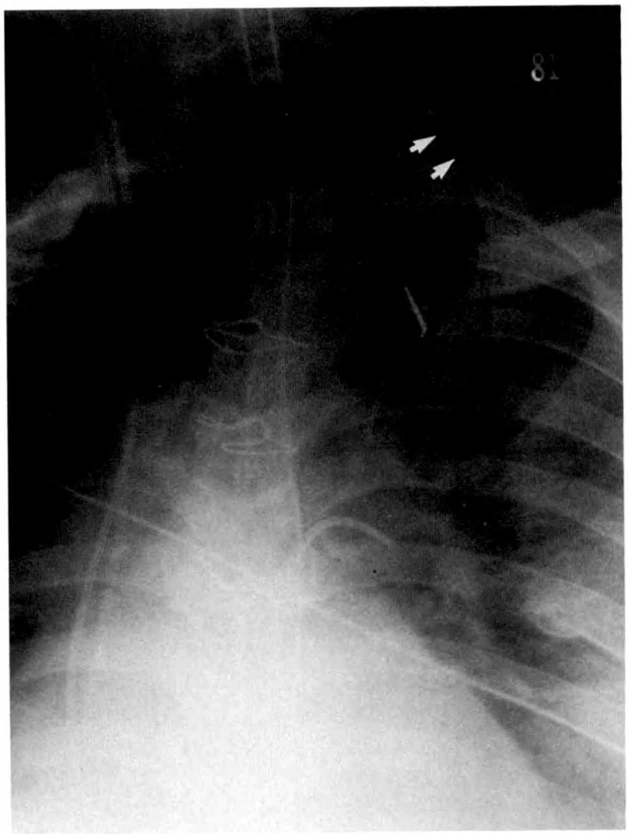

Fig 1. (Patient 6, 72-year-old man.) Supine anteroposterior chest radiograph. There is an oblique fracture (arrows) *of the left first rib at the costotransverse articulation.*

The mechanism of fracture is most likely that of an indirect force applied to the ribs secondary to sternal retraction. Additional stress is placed on the left upper ribs if the internal mammary artery is used for grafting. It is noteworthy that in 46% of the patients in whom this complication developed the left internal mammary artery was used. The position of the sternal retractor has also been implicated in the development of rib fractures. Vander Salm and associates [6] have demonstrated in cadavers that the incidence of fractures can be decreased by placing the crossbar caudally and the upper blade at the fourth intercostal space rather than at the second. Because there was no correlation between operating room time, bypass time, or cross-clamp time and the development of fractures, the fractures probably occurred during the initial retraction of the sternum. This may explain why the fractures occurred in the heavier patients and those with larger body surface areas, where a wider exposure is necessary relative to body habitus.

Most of the fractures occur posteriorly and involve the left first rib [4, 5]. They tend to be asymptomatic but may

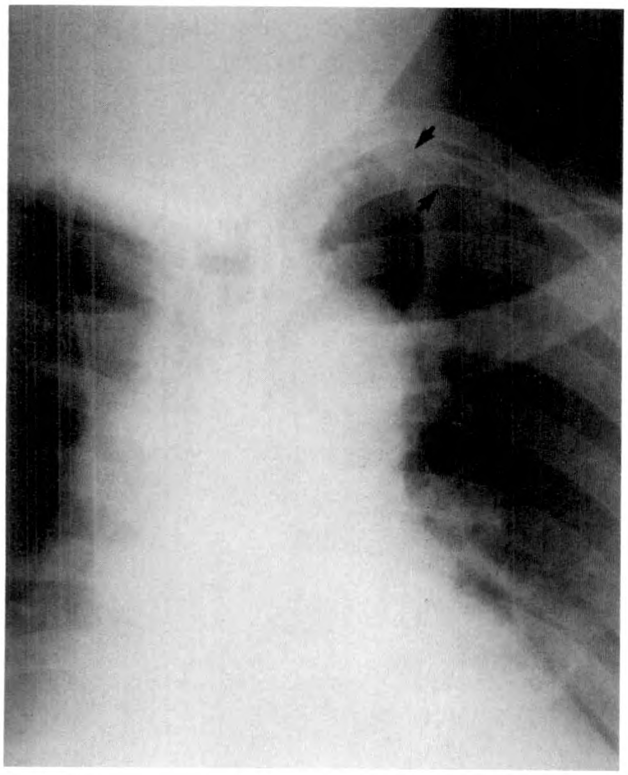

Fig 2. (Patient 7, 64-year-old man.) Supine anteroposterior chest radiograph. Comminuted fracture (arrows) *of the midshaft of the left first rib is identified.*

be associated with neck, chest, or shoulder pain. This poses a dilemma in these postoperative patients, in whom the symptoms may suggest angina pectoris, myocardial infarction, pulmonary embolism, or postpericardiotomy syndrome [2, 4, 5]. The primary care physician must be aware of this complication of median sternotomy and should attempt to reproduce the symptoms by palpating the appropriate ribs before subjecting the patient to additional testing to rule out these more serious entities. Brachial plexus palsies may also develop postoperatively and may be related to stretching of nerves [4] or impingement upon the plexus by the fractured first rib [6].

Table 3. Categorical Characteristics

Variable	Fracture (No.)	No Fracture (No.)	p Value[a]
Sex			0.372
F	5	45	
M	8	42	
Procedure			0.242
CABG	12	69	
Other	1	18	
LIMA	6	29	0.272
Prior sternotomy	2	5	0.225
Reexploration	3	7	0.250
30-day mortality	0	5	0.491

[a] Chi-square analysis with Fischer's exact test for numbers.

CABG = coronary artery bypass grafting; LIMA = left internal mammary artery.

Table 4. Continuous Characteristics[a]

Variable	Fracture	No Fracture	p Value[b]
Age (y)	62.08 ± 11.41	57.13 ± 13.58	0.2158
Height (cm)	169.69 ± 10.93	166.71 ± 10.2	0.3328
Weight (kg)	85.69 ± 16.38	76.75 ± 16.38	0.0713
Body surface area (m^2)	1.93 ± 0.25	1.81 ± 0.21	0.0771
Body mass index (kg/m^2)[c]	29.9 ± 6.5	27.3 ± 5.6	0.1437
Ischemic time (min)	49.30 ± 14.08	54.26 ± 20.79	0.4088
Bypass time (min)	106.08 ± 25.6	103.74 ± 47.91	0.7914
Operating room time (min)	378.38 ± 121.65	384.13 ± 111.87	0.8648

[a] Values are shown as mean ± standard deviation. [b] Student's t test. [c] Weight in kilograms/(height in meters)^2.

These fractures may be very subtle, can be overlooked initially, and may not be radiographically visible even in retrospect. In the series of Greenwald and associates [5], only 4 of 44 fractures identified by radionuclide imaging were noticeable on the chest radiographs, 1 initially and 3 retrospectively. Similarly, the fractures were missed initially in 4 of our patients (patients 1, 2, 10, and 13). Portable postoperative chest radiographs are not ideal for displaying bone detail, and in addition, the thoracic cage is frequently obscured by the various support devices to which the patient is attached. Radiographs of the cervical spine [2, 6] and radionuclide bone images [5] can be used to demonstrate suspected fractures when the chest radiograph is negative and patients are clinically stable.

In summary, we have found fractures to the upper ribs to occur in 13% of patients undergoing median sternotomies. Obese patients and those with larger body surface areas are more susceptible to this complication. Even in these patients, however, careful attention to appropriate placement of the sternal retractor will decrease the occurrence of rib fractures. A much larger sample size would be needed to statistically validate other predisposing factors. Fractures should be suspected in patients complaining of neck, chest, or shoulder pain in whom no other cause can be found.

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References

1. Sanfelippo PM, Danielson GK. Complications associated with median sternotomy. J Thorac Cardiovasc Surg 1972;63:419–23.
2. Curtis JA, Libshitz HI, Dalinka MK. Fracture of the first rib as

a complication of midline sternotomy. Radiology 1975;115:63-5.
3. Carter AR, Sostman HD, Curtis AM, Swett HA. Thoracic alterations after cardiac surgery. AJR 1983;140:475-81.
4. Woodring JH, Royer JM, Todd EP. Upper rib fractures following median sternotomy. Ann Thorac Surg 1985;39:355-7.
5. Greenwald LV, Baisden CE, Symbas PN. Rib fractures in coronary bypass patients: radionuclide detection. Radiology 1983;148:553-4.
6. Vander Salm TJ, Cereda JM, Cutler BS. Brachial plexus injury following median sternotomy. J Thorac Cardiovasc Surg 1980;80:447-52.

REVIEW OF RECENT BOOKS

Thoracic Surgery
Edited by H. Pichelmaier and F. W. Schildberg
Berlin, Heidelberg, Springer-Verlag, 1989
460 pp, illustrated, $375.00

Reviewed by Steven W. Guyton, MD

This overview of the procedures included in noncardiac thoracic surgery provides the reader with a vision of the broad operative scope of this specialty. A short chapter on operations of the breast is included. More than half of the text is devoted to procedures on the esophagus.

Brief treatises on pathophysiology, general surgical technique, and indications for operation are followed by detailed descriptions of common procedures. The text is extensively illustrated, giving more the feel of a surgical atlas than a textbook.

In addition to the well-illustrated text a separate section of anatomical plates covering the neck, chest wall, and intrathoracic anatomy serves as an aid in understanding the discussion of operative steps. These plates are situated in the back of the book in such a way that they can be folded out and referred to as the text is read.

Only a very small portion of the book is devoted to assessment of operability and perioperative management. The discussions of these subjects are sketchy but give a reasonably practical overview of functional operability, parenteral nutrition, perioperative antibiotics, and chest physiotherapy.

The remaining 95% of the book is devoted to surgical instruments, materials and approaches, and operations and procedures. For discussing the various operative procedures a standard format is generally used that enumerates (1) preoperative preparation, (2) instruments, (3) patient position, (4) surgical approach, and (5) operative technique. Separate highlighted boxes reduce the operative steps to a condensed outline form. Indications and potential complications are included in the text or under separate headings.

Cross-references to section numbers in the chapter on surgical incisions are frequently incorrect, sometimes causing distinct confusion in trying to follow discussion of a surgical approach.

The detailed technical description of operative procedures is the book's greatest asset. The greater space devoted to esophageal procedures allows more in-depth description of disease processes, reflection on the contributions of surgical pioneers in the field, and discussion of alternative approaches to therapy.

This text is an excellent introduction to thoracic surgical procedures for the student or resident involved in the operative management of these patients. It is a useful reference for the practicing thoracic surgeon, particularly for review preoperatively of technically demanding though perhaps infrequently performed procedures. My concern is that the book should not be considered a text covering the broad area of "Thoracic Surgery" as is the title on the cover, but is more appropriately described by the subtitle found only on the title page—"Surgical Procedures on the Chest and Thoracic Cavity."

Seattle, Washington

Randomized Trial of One-Dose Versus Six-Dose Cefazolin Prophylaxis in Elective General Thoracic Surgery

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The objective of this study was to compare the efficacy of one to six doses of cefazolin as prophylaxis in general thoracic surgery using a randomized, double-blind design. Two-hundred eight consecutive patients admitted to a regional thoracic surgery unit for elective thoracotomy and lung resection were eligible for the trial. There were no wound infections in the one-dose group and two in the six-dose group (95% confidence intervals [CI]: −0.008, +0.048 [The positive number refers to the largest possible difference in favor of the one-dose group and the negative number, the largest possible difference in favor of the six-dose group]). Each group had eight postoperative chest infections (CI: −0.075, +0.077) and three empyemas (CI: −0.004, +0.050). Thirty-day mortality was 5% in the one-dose group and 4% in the six-dose group (CI: −0.053, +0.069). Postoperative duration of hospital stay, requirement for antibiotics, and the need for reoperation were comparable. These results suggest that six doses of cefazolin do not confer clinically important benefit beyond that obtained from a single dose for prophylaxis of wound infection in elective general thoracic surgery.

(Ann Thorac Surg 1991;51:956–8)

Whereas surgeons agree that aseptic technique is of paramount importance in preventing morbidity from postoperative infection, most also agree that antibiotic prophylaxis will further reduce its incidence in some surgical settings. The results of randomized trials suggest that antibiotic prophylaxis can reduce postoperative wound infection in patients undergoing elective general thoracic surgical procedures [1–3]. There is no consensus, however, regarding the most appropriate duration of prophylaxis. Recent trials in general surgery have demonstrated that a single preoperative dose of antibiotic is as effective as longer prophylactic schedules [4].

The present prospective, double-blind, randomized clinical trial was designed to assess the efficacy of prophylaxis with a single preoperative dose of cefazolin in elective general thoracic surgery compared with a six-dose perioperative regimen. In addition, the incidence of postoperative chest infection, empyema, other infection, and 30-day mortality was ascertained, accepting that prophylaxis is administered primarily to reduce the incidence of wound infection.

Material and Methods

Patients

Two hundred eight consecutive patients admitted to the Regional Thoracic Surgery Unit, Frenchay Hospital, and scheduled for thoracotomy and lung resection between August 1, 1987, and November 30, 1988, were eligible for inclusion in the trial. Patients who had (1) penicillin or cephalosporin allergy, (2) received antibiotics within 7 days of operation, (3) valvular heart disease requiring prophylaxis against bacterial endocarditis, or (4) concomitant infection were excluded.

Regimens

All eligible patients were randomized according to a schedule of random numbers that had been generated by the hospital pharmacy. Patients received either one dose of cefazolin (1 g intravenously [IV]) at induction of anesthesia and five doses of intravenous placebo at 8-hour intervals thereafter or one dose of cefazolin (1 g IV) at induction of anesthesia and five further doses (1 g IV) every 8 hours. For patients whose operation exceeded 3 hours' duration, an additional intraoperative dose of cefazolin (1 g IV) was administered.

The preoperative dose of cefazolin was drawn up in a syringe and administered by either the anesthetist or the surgical staff; five subsequent doses of drug or placebo, having been prepared by the pharmacy in identically appearing 50-mL bags numbered 2 through 6, were administered by the nursing staff.

The operative site was routinely shaved 12 to 18 hours preoperatively and patients had one bath without special antiseptic soap within the 12 hours before their operations. Both 1% iodine in 70% methylated spirit and 0.5% chlorhexine in 70% methylated spirit were used for preoperative skin preparation. Opsite (Smith-Nephew) was used routinely to cover the operative field. Surgical tech-

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nique was standardized as far as possible, with all resections being performed by two surgical teams. Airstrip dressing (Smith-Nephew, Hull, UK) or Nobecutane Plastic Wound Spray plus Mefix self-adhesive dressings (Molnlycke, Dunstable, UK) were used to cover the skin incision at the conclusion of each operation. The original dressing remained for 48 hours postoperatively, at which time the wounds were left open to air.

The pleural space was drained postoperatively for 24 to 48 hours in pneumonectomy patients and for 72 to 96 hours in lobectomy patients. Chest roentgenograms were taken daily until the chest drains had been removed, on the day before discharge, and at the 6-week postoperative visit.

Surveillance and Follow-up

After operation, all patients were evaluated twice daily until discharge and again at the 6-week postoperative visit by the registrar for evidence of postoperative fever, wound infection, chest infection, empyema, or other infection. Definitions of each event are as follows: *fever*: an oral temperature of 38°C or greater recorded on at least 2 successive occasions more than 6 hours apart, excluding the first 24 hours after operation; *wound infection*: any wound that discharged, spontaneously or otherwise, purulent material with or without culture of a pathogen; *chest infection*: sputum culture demonstrating heavy growth of a pathogenic organism or two of the following findings: fever, purulent sputum, an infiltrate on chest, or auscultatory evidence of pulmonary consolidation; *empyema*: recovery of purulent material from the pleural cavity with or without culture of pathogen.

Sputum was cultured preoperatively for patients with productive cough, and the bronchial stump was cultured when technically possible. Sputum, chest drainage, wound, urine, and blood cultures were taken as indicated by the patient's clinical postoperative course.

The length of preoperative stay, operation, and postoperative stay were recorded. Patients who required secondary operative procedures as well as those with prolonged air leaks were noted. The 30-day and hospital mortality rates were recorded as was any adverse reaction to the prophylaxis.

Analysis

All results were tabulated and statistical analysis was performed. Confidence limits on the difference in proportion of each event in the one-dose versus six-dose groups were calculated with use of the normal approximation to the binomial distribution.

Results

Two hundred eight eligible patients were randomized in the study. Nine patients were excluded from data analysis because they missed one or more dose(s) of the study drug (n = 4) or because a previously undiagnosed infection was discovered at the time of operation (n = 5). The decision to exclude a patient was made before breaking the code in every instance. A total of 199 patients were randomized, 100 to the six-dose group and 99 to the one-dose group. One patient in each group received an intraoperative dose of cefazolin (1 g IV) because their operation exceeded 3 hours' duration.

Demographic characteristics of the two groups are presented in Table 1 and demonstrate their comparability with respect to age, sex, and primary diagnosis.

The extent of operation was similar in the one-dose and six-dose groups: pneumonectomy was performed in 25% and 28%, and lobectomy in 53% and 51%, of patients in the two groups, respectively. Mean operating time was 124 and 125 minutes in the one-dose and six-dose groups, respectively (Table 2).

Two wound infections occurred, both in the six-dose

Table 1. Demographic Characteristics of the One-Dose and Six-Dose Groups

Variable	One-Dose Group	Six-Dose Group
Number	99	100
Percentage male	70	72
Mean age (y)	62.6	63.5
Diagnosis[a]		
Primary lung carcinoma	76	76
Metastatic carcinoma	5	6
Benign disease	16	17
Type of operation		
Pneumonectomy	25	28
Lobectomy/bilobectomy	53	51
Wedge/segmental resection of lung	9	9
Thoracotomy ± biopsy	12	12

[a] The final pathology of 2 patients in the one-dose group and 1 in the six-dose group was not available.

Table 2. Results

Variable	One-Dose Group (n = 99)	Six-Dose Group (n = 100)	95% CI[a]
Wound infection	0	2	−0.008, +0.048
Chest infection	8	8	−0.075, +0.077
Empyema	3	3	−0.004, +0.005
Operating time (min)			
Mean	124	125	
Range	60–240	45–240	
Postop hospital stay (d)			
Mean	13.7	13.4	
Range	6–49	3–52	
Postoperative antibiotic requirement (No.)	12	13	
Reoperation (No.)	3	4	

[a] 95% confidence intervals on the difference in proportion of infection; the negative number refers to the largest possible difference in favor of the six-dose group. The positive number refers to the largest possible difference in favor of the one-dose group.

group. Eight chest infections and three empyemas occurred in each group. The 95% confidence intervals on the difference in the proportion of these infectious events in the two groups are narrow (see Table 2).

The mean duration of hospital stay, as well as the number of patients requiring postoperative antibiotics or reoperation, are presented in Table 2. The table demonstrates comparability of the groups with respect to these variables. No additional wound infections were recorded at 6-week postoperative follow-up.

There were five deaths (5/99, 5%) in the one-dose group and four deaths (4/100, 4%) in the six-dose group at 30 days.

The results show no differences between the groups in a number of outcomes. The primary outcome, wound infection, shows a trend in favor of the one-dose group. Differences between groups did not, however, approach statistical significance for any variable assessed.

We can thus state with 95% confidence that one dose of prophylactic cefazolin will result in no greater than a 4.8% reduction in wound infection compared with six doses and, furthermore, that six doses will result in a no greater than 0.8% reduction in wound infection compared with a single dose.

Comment

In this study of antibiotic prophylaxis for patients undergoing elective thoracotomy and lung resection the wound infection rate was 1%, which is lower than most [1–3] but not all [5] other published reports. A chest infection rate of 8% and an empyema rate of 3% are comparable with previous reports [1, 3, 5]. Likewise, a 30-day mortality rate of 4.5% is comparable with previous reports [1, 5].

It became apparent from the finding of a total of only two wound infections in the first 199 patients randomized that a much larger number of patients would need to be entered into the trial than had been calculated based on previously published wound infection rates to demonstrate the lack of a statistically significant difference between the two groups. By calculating 95% confidence intervals of the difference in the proportion of various events in the two groups, however, we were able to come to several conclusions.

The most relevant confidence limit is that which defines the largest proportion of patients who might benefit from a six-dose prophylaxis schedule. For wound infections and empyema the data exclude clinically important differences in favor of the six-dose group. At most, six-dose cefazolin prophylaxis will benefit 8 and 4 patients in a thousand, respectively, for these two variables.

The results of this trial strongly suggest that six doses of parenteral cefazolin do not confer clinically important benefit beyond that obtained from a single dose as prophylaxis in elective general thoracic surgery. Aside from the clinical result, the cost of five additional doses of the drug, pharmacy preparation costs, the cost in terms of nursing time, and the cost to patients in terms of the necessity for an intravenous line to be maintained for 48 hours postoperatively should encourage clinicians to alter their prophylaxis schedule in favor of a single-dose regimen.

The low overall wound infection rate compared with other trials conducted in the last decade [1, 3] raises the question of whether or not antibiotic prophylaxis for elective general thoracic surgery is required at all. This question merits evaluation as a secondary outcome within the context of a future clinical trial.

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References

1. Ilves R, Cooper JD, Todd TR, Pearson FG. Prospective, randomized, double-blind study using prophylactic cephalothin for major, elective, general thoracic operations. J Thorac Cardiovasc Surg 1981;81:813–7.
2. Kvale PA, Ranga V, Kopacz M, Cox F, Magilligan DJ, Davila JC. Pulmonary resection. South Med J 1977;70(Suppl 1):64–8.
3. Fridmodt-Moller N, Ostri P, Pedersen IK, Poulsen SR. Antibiotic prophylaxis in pulmonary surgery—a double-blind study of penicillin versus placebo. Ann Surg 1982;195:444–50.
4. Kaiser AB. Antimicrobial prophylaxis in surgery. N Engl J Med 1986;325:1129–38.
5. Tarka M, Pokela R, Lepojarvi M, Nissinen J, Karkola P. Infection prophylaxis in pulmonary surgery: a randomized prospective study. Ann Thorac Surg 1987;44:508–13.

Spinal Cord Protection During Aortic Occlusion: Efficacy of Intrathecal Tetracaine

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Spinal cord ischemia and resultant paraplegia are devastating sequelae in up to 40% of patients undergoing repair of thoracoabdominal aneurysms. We investigated the effect of intrathecal tetracaine on the neurological sequelae of spinal cord ischemia and reperfusion with aortic occlusion. Cocaine-derived anesthetics (lidocaine and its analogues) have been shown to decrease neuronal cell metabolism and also have specific neuronal membrane stabilizing effects. New Zealand white rabbits were anesthetized and spinal cord ischemia was then induced by infrarenal aortic occlusion. Animals were divided into six treatment groups. Tetracaine (groups 2 and 4) or normal saline solution (group 5) was administered intrathecally before aortic cross-clamping. Groups 1 and 3 functioned as controls. Group 6 animals received intravenous thiopental. Rabbits were classified as either neurologically normal or injured (paralyzed or paretic). Among controls, 25 minutes of aortic occlusion produced varied neurological sequelae (group 1, 3/6 injured, 50%) whereas 30 minutes resulted in more consistent injury (group 3, 5/6 injured, 83%). All rabbits that received intrathecal saline solution were paralyzed (group 5, 4/4 injured, 100%). Animals treated with intrathecal tetracaine and aortic occlusion of 30 minutes (group 4) showed significantly better preservation of neurological function (6/7 normal, 86%) than controls and saline-treated animals (groups 3 and 5). All animals treated with intrathecal tetracaine and aortic occlusion for 25 minutes (group 2) showed no signs of injury (5/5 normal, 100%), but this was not significant versus controls (group 1). Intravenous thiopental (group 6, 5/5 injured, 100%) had no beneficial effect. Intrathecal tetracaine significantly and dramatically abrogated the neurological injury secondary to spinal cord ischemia and reperfusion after aortic occlusion at 30 minutes in the rabbit model.

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Spinal cord ischemia and resultant paraplegia are devastating sequelae in approximately 11% of patients undergoing elective descending thoracic and thoracoabdominal aneurysm repair and nearly 40% undergoing emergent repairs and dissections [1]. Many interventions designed to circumvent this complication have been implemented in laboratory and clinical models without clear benefit. Cerebrospinal fluid (CSF) drainage had initially shown promise in animal models; however, Crawford and associates [2] recently showed no protective benefit of cerebrospinal fluid drainage in a clinical prospective, randomized trial. Cocaine-derived anesthetics, including tetracaine, have been shown to be effective in decreasing the metabolic rate of the neuronal cell. Through their anesthetic effect on the sodium/potassium pump, cocaine-derived anesthetics also inhibit ion fluxes and thus stabilize the neuronal cell membrane. These anesthetics may prolong spinal cord ischemic tolerance by decreasing metabolic demand. We investigated the effect of intrathecal tetracaine on the neurological sequelae of spinal ischemia and reperfusion injury secondary to aortic occlusion in the rabbit model.

Material and Methods

Forty-three adult New Zealand white rabbits (2.8 to 4.9 kg; mean, 3.6 kg) were divided into six treatment groups designated 1 to 6. Six animals died before recovery and neurological assessment and were not included in the study. Four other animals were not included owing to inability to obtain intrathecal access. The animals in groups 1 and 3 were designated controls and were initially sedated with 0.3 mL of intramuscular xylazine (100 mg/mL), then anesthetized with 1.3 mL ketamine/acepromazine maleate solution (0.09 mg/mL acepromazine with 9.1 mg/mL ketamine) intramuscularly. Further maintenance anesthesia was accomplished with sparing amounts of intravenous Nembutol (5 mg/mL). No hypothermia was induced and each procedure was performed in the same operating room at ambient temperature. Blood pressure was not monitored owing to the animal's small size and to the need for complete anesthetic recovery of the rabbit. Each animal underwent laparotomy through a midline incision after local skin infiltration with 0.5% Xylocaine. The external iliac vessels were isolated bilaterally and doubly looped with 3-0 silk ties. The abdominal contents were then reflected to the right and the abdominal aorta

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Table 1. Experimental Results

Variable	Group 1 (Control, n = 6)	Group 2 (Tetracaine, n = 5)	Group 3 (Control, n = 6)	Group 4 (Tetracaine, n = 7)	Group 5 (Saline, n = 4)	Group 6 (Thiopental, n = 5)
Ischemic Time (min)	25	25	30	30	30	30
Neurological Condition						
Normal	3 (50%)	5 (100%)	1 (17%)	6 (86%)[a]	0	0
Paretic	2 (33%)	0	0	1 (14%)	0	1 (20%)
Paralyzed	1 (17%)	0	5 (83%)	0	4 (100%)	4 (80%)

[a] $p < 0.05$ versus groups 3, 5, and 6.

was isolated just distal to the left renal artery. A silk tie was placed loosely around the aorta and the aorta was cross-clamped at this level. The ties around the iliac vessels were tightened and the aorta was palpated to confirm loss of pulse. The cross-clamp time for group 1 was 25 minutes and for group 3, 30 minutes. The cross-clamp was released at the designated time and the silk ties were removed. The laparotomy incision was closed in two layers and the animal allowed to recover.

After initial anesthesia of 0.3 mL xylazine and 1.3 mL ketamine only, the animals of groups 2 and 4 were placed in the left lateral position. No acepromazine was given at this point due to its long half-life. After local skin infiltration with 0.5% Xylocaine an incision was made through the skin overlying the lumbar spine. Penetration of the intrathecal space was then carried out between L2 and L5 using a 25-gauge spinal needle. Once CSF was obtained, the intrathecal space was injected with 0.3 mL 1% tetracaine. No drainage of CSF was performed. The posterior incision was then closed and the animal allowed to recover for 1 to 2 hours to determine the result of the intrathecal anesthetic. All animals were noted to have no lower extremity function. Once the effect of tetracaine was confirmed, the animal was resedated with 1.3 mL of intramuscular ketamine/acepromazine maleate, and laparotomy was performed as described for groups 1 and 3. The cross-clamp time was 25 minutes for group 2 and 30 minutes for group 4.

The animals of group 5 were initially sedated with 0.3 mL of xylazine and anesthetized with 1.3 mL of ketamine as in groups 2 and 4. Intrathecal access was achieved and the intrathecal space injected with 0.3 mL of normal saline solution. The animal was then allowed to recover to assess neurological status. All animals were noted to have normal lower extremity function. The animal was then reanesthetized and laparotomy performed in the manner previously described. Cross-clamp time was 30 minutes in group 5.

The rabbits of group 6 were sedated with acepromazine and anesthetized with ketamine/xylazine. Tracheostomy was performed and the rabbit was placed on a Bodine mechanical ventilator at a rate of 20 respirations/min × 25 mL tidal volume on room air. Thiopental (20 mg/kg) was administered intravenously over 20 to 30 minutes. Thirty minutes after initial administration of thiopental, aortic occlusion was performed in the manner described.

Once the rabbits had adequately recovered from anesthesia, neurological status was assessed 6 to 10 hours after aortic cross-clamping. "Neurological status" was graded as, (1) normal (able to hop), (2) paralyzed (unable to hop with no lower extremity movement), and (3) paretic (unable to hop but with some lower extremity movement). The animals were killed after neurological evaluation. Animal care and all procedures were performed in compliance with the NIH "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985). Comparisons were made by classifying rabbits as either neurologically normal or injured (paralyzed or paretic). Statistical evaluation was performed using the Fisher exact test with correction. Differences between groups were considered significant at a p value of less than 0.05.

Results

Our results are presented in Table 1.

Controls (Groups 1 and 3)

Twenty-five minutes of aortic occlusion produced varied results (3/6 injured, 50%) in group 1 controls. Thirty minutes of aortic occlusion resulted in more consistent injury in group 3 controls (5/6 injured, 83%).

Intrathecal Tetracaine (Groups 2 and 4)

Twenty-five minutes of aortic occlusion had no clinical effect on neurological function in group 2 with 100% (5/5) of animals having normal neurological function. This was not significant versus 25-minute controls ($p = 0.12$). Thirty minutes of aortic occlusion in group 4 resulted in 86% (6/7) of animals with normal neurological function. This was significant versus the 30-minute control group 3 ($p < 0.03$).

Intrathecal Saline Solution (Group 5)

All (4/4, 100%) animals given the intrathecal saline placebo were paralyzed after 30 minutes of aortic occlusion. This was significant versus the intrathecal tetracaine group 4 ($p < 0.02$).

Intravenous Thiopental (Group 6)

All (5/5, 100%) animals given intravenous thiopental exhibited neurological injury after 30 minutes of aortic occlusion. This was again significant versus the intrathecal tetracaine group 4 ($p < 0.01$).

Comment

Aortic occlusion produces several detrimental effects on spinal cord perfusion. In humans and experimental animals, organs distal to an aortic cross-clamp are poorly supplied by blood unless collateralization has occurred, as in coarctation of the aorta. Thus, the spinal cord is poorly supplied through the radicular medullary arteries arising from the segmental aortic branches or from the longitudinal spinal arteries including the anterior spinal artery. Cerebrospinal fluid pressure may increase secondary to proximal hypertension and homeostatic reflexes [3]. These two changes result in decreased spinal cord perfusion and ischemia [4].

The rabbit, baboon, and dog have all been used as models for spinal cord ischemia. In the rabbit the major segmental artery blood supply to the spinal cord arises from the infrarenal aorta. Therefore, infrarenal aortic occlusion will induce spinal ischemia. This makes the rabbit a relatively simple model for study as thoracotomy is avoided. In the dog and baboon collateral flow arises from the aorta between T7 and T12 and thoracotomy is necessary to cross-clamp this aortic segment.

Numerous interventions designed to safely extend the period of aortic occlusion have been attempted in the rabbit, in other animal models, and in humans. Each intervention has been targeted at a specific point in the spinal ischemic cascade described.

Shunts

Aortoaortic shunting and cardiopulmonary bypass during thoracic aortic occlusion have been described extensively as a means of improving spinal artery pressure and perfusion. The incidence of paraplegia was decreased in animal studies with shunting [5]. Enthusiasm for shunting has diminished since Crawford and Rubio [6] published their experience with and without shunting for aneurysm repair. Crawford and Rubio found no significant difference in paraplegia rates between groups of patients who were shunted and those not shunted. Given the increased morbidity associated with shunting, they did not recommend it as standard therapy. Shunting may play a role in patients who require extensive aortic resection [7].

Cerebrospinal Fluid Drainage

Cerebrospinal fluid drainage has been proposed as a method of spinal cord protection during aortic occlusion. The effect of CSF drainage is to lower CSF pressure and thus vascular resistance, theoretically increasing spinal cord perfusion. Cerebrospinal fluid drainage should also alleviate the effects of spinal cord edema after ischemic injury as the cord will be able to expand into the canal more readily. Decreased paraplegia rates have been reported clinically as well as from the laboratory [8]. Crawford and associates [2] recently reported that paraplegia rates were no different between patients treated with and without CSF drainage in a randomized, prospective clinical trial.

Pharmacological Manipulation

Pharmacological methods of obviating reperfusion injury in spinal cord ischemia are well described. Drug interventions investigated include free radical scavengers, opiate antagonists, and membrane-stabilizing agents such as corticosteroids and barbiturates. Superoxide dismutase had been shown to have some protective effect, but more recent data reveal no significant improvement in neurological function in either the canine or rabbit model [9–11]. Intravenous thiopental administered 30 minutes before cross-clamping has been reported to be advantageous, but other studies and our data do not corroborate these findings [10, 11].

Corticosteroids

Administration of intravenous corticosteroids before and after ischemic injury is thought to prevent neuronal damage and hence paraplegia. The method of action proposed includes blunting of the postischemic inflammatory response by decreasing spinal cord edema, free radical scavenger activity, and membrane stabilization effects. Laschinger and co-workers [12] found no neurological injury secondary to spinal ischemia in dogs pretreated with corticosteroids. Subsequent studies revealed no benefit with intravenous steroids alone [13]. Fowl and colleagues [14] found significant improvement in neurological function in rabbits administered preoperative and postoperative U-74006F, a newly derived 21-aminosteroid with stabilizing effects on the lipid portion of the cellular membrane. Further study is warranted.

Opiate Antagonists

Over the past 10 years much investigative work has focused on the role of endogenous opioids and excitatory amino acids in reperfusion injury. Nalmafene, an opiate receptor antagonist, and MK-801, an antagonist to the *N*-methyl-D-aspartate subtype of excitatory amino acid receptors, have been effective in decreasing the inflammatory response. Yum and Faden [15] administered each agent intravenously to rabbits in a spinal ischemia model. The nalmafene- and MK-801–treated rabbits showed a 53% and 40% normal neurological result after injury, respectively, which was significantly greater than controls. No further studies have been performed to support or disclaim their research.

Intrathecal Papaverine

The only intrathecal pharmacological intervention in the spinal cord ischemia model is that of Svensson and associates [16, 17]. They noted significant improvement in the frequency of neurological injury in baboons and humans with cerebrospinal fluid drainage and intrathecal administration of papaverine. Dilatation of the anterior spinal artery and improved spinal cord blood flow was reported in baboons with resultant decreased incidence of paraplegia. A small trial of 11 patients undergoing thoracoabdominal aneurysm repair with intrathecal papaverine

Table 2. Multimodal Therapy

First Author	Intervention	Model	% Recovery of Function
Robertson [19]	Hypothermia, thiopental	Rabbit	75%
Kirshner [10]	Cold perfusion, superoxide dismutase, thiopental	Dog	50%
Woloszyn [13]	Cerebrospinal fluid drainage, steroids	Dog	83%

and CSF drainage revealed no early paraplegia with no morbidity secondary to papaverine. Further trials are warranted to substantiate the clinical benefit of this agent.

Hypothermia

Hypothermia has been shown to decrease cellular metabolism and energy consumption in the cellular model [18]. Robertson and associates [19] noted a significant increase in the ischemic threshold tolerated in the rabbit model in both whole body and local hypothermia. Others have noted no improvement with hypothermia alone [10].

Multimodal Therapy

Several investigators have combined different interventions to prevent spinal cord injury with aortic occlusion (Table 2). Multimodal therapy does appear to improve the neurological result in these earlier studies. When each single intervention was used independently, no significant improvement over controls was noted. Therefore, combination therapy may enhance the efficacy of one agent.

Cocaine-Derived Anesthetics

Lidocaine and its effects on neuronal cell metabolism and neuron injury have been the object of much investigation. As early as 1956 the effects of cocaine-derived local anesthetics on rat brain cells were described. A reduction of cell respiration with tetracaine was noted by Geddes and Quastel [20]. Lidocaine and its analogues have been reported to reversibly inhibit electron transport and uncouple oxidative phosphorylation on porcine brain mitochondria [21]. In addition, lidocaine has a stabilizing effect on neuronal cell membranes due to its action of blocking the sodium/potassium pump and preventing potassium ion fluxes across the cell membrane [18, 22]. In the acute cerebral ischemia model, lidocaine has been shown to improve recovery of somatosensory evoked potentials after ischemia. Benefit was achieved if the anesthetic was administered either before or after the ischemic event [23].

There has only been one trial in which the efficacy of lidocaine has been assessed in preventing spinal cord ischemia [19]. Robertson and co-workers delivered 160 mg/kg lidocaine intravenously in a rabbit model followed by aortic occlusion 15 minutes later. No benefit was noted in their experiments, with a 60% paraplegia rate in the 25-minute ischemia group. Failure was postulated to be secondary to hypotension after systemic administration. An inability to reach protective concentrations in the CSF could also have contributed to the failure of intravenous lidocaine.

In reviewing other investigators' work using the rabbit model for spinal ischemia, there appears to be a variation in what the "ischemic threshold" period of aortic occlusion is to produce consistent neurological injury. Consistent paralysis in our study was produced after 30 minutes of infrarenal occlusion. Yum and Faden [15] noted the ischemic threshold to be 16 minutes; Fowl and associates [14], 25 minutes; Robertson and colleagues, 40 minutes; and Gerhardt and co-workers [11], 27 minutes. Variance in this time period can be accounted for by differences in operative technique, different routes of anesthesia, or different anesthetic agents. What would appear most important is visualization of the takeoff of the left renal artery to allow proper placement of the aortic cross-clamp and thus exclusion of infrarenal segmental lumbar arteries that supply the spinal cord. In each study, including ours, there is a consistent 10% to 20% incidence of rabbit controls that do tolerate the ischemic threshold of aortic occlusion and have normal postischemic neurological function: 1 of 7 controls (14%) in group 3 had normal neurological function after ischemia. Variety in collateral arterial flow to the anterior spinal artery in the rabbit can best account for this discrepancy. Technique aside, what is most important when comparing studies of spinal cord ischemia is to determine the relative improvement in neurological function in treatment groups over the ischemic threshold in each individual study. If one then evaluates and compares the results of pretreatment with intrathecal tetracaine (86% normal) versus other single treatments, namely nalmafene (53% normal), MK-801 (40% normal), and U-74006F (56% normal), intrathecal tetracaine fares favorably as a single therapeutic agent in the rabbit model. Multimodal therapy as noted in Table 2 has shown significant benefit as well. A regimen of intrathecal tetracaine in conjunction with some other intervention may provide even better results.

Conclusions

Intrathecal tetracaine significantly and dramatically abrogated the neurological injury secondary to spinal cord ischemia and reperfusion after aortic occlusion at 30 minutes in the rabbit. Intrathecal saline solution and intravenous thiopental had no effect. The protective effects of intrathecal tetracaine may stem from its suppression of cellular metabolism and from its stabilization of the neuronal cell membrane. Prior failure to demonstrate beneficial effect of intravenous lidocaine in previous studies may be secondary to hypotension from systemic administration and inability to reach protective concentrations in the CSF. Our results compare favorably with other single-agent interventions in the rabbit model. Although extrapolating the results to humans is premature, intrathecal tetracaine may prove to be a simple yet effective means of spinal cord protection in thoracoabdominal aneurysm repair, either alone or in conjunction with other agents. Further studies are in progress.

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References

1. Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. J Vasc Surg 1986;3:389–402.
2. Crawford ES, Svensson LG, Shenaq SS, et al. A prospective randomized study of cerebrospinal fluid drainage to prevent paraplegia after high risk surgery on the thoracoabdominal aorta. Presented at the 44th Scientific Meeting of the Society for Vascular Surgery, June 4, 1990.
3. Spence PA, Lust RM, Sun YS, et al. Prevention of reflex-mediated increases in cerebrospinal fluid pressure during aortic surgery. Surg Forum 1990;41:297–9.
4. Hollier LH, Marino RJ. Thoracoabdominal aortic aneurysms. In: Moore WS, ed. Vascular surgery: a comprehensive review. 3rd ed. Philadelphia: W.B. Saunders, 1991:301.
5. Svensson LG, Rickards E, Coull A, et al. Relationship of spinal cord blood flow to vascular anatomy during thoracic aortic crossclamping and shunting. J Thorac Cardiovasc Surg 1986;91:71–8.
6. Crawford ES, Rubio PA. Reappraisal of adjuncts to avoid ischemia in the treatment of aneurysms of descending thoracic aorta. J Thorac Cardiovasc Surg 1973;66:693–704.
7. Kouchoukos NT, Wareing TH, Izumoto H, Klausing W, Abboud N. Elective hypothermic cardiopulmonary bypass and circulatory arrest for spinal cord protection during operations on the thoracoabdominal aorta. J Thorac Cardiovasc Surg 1990;99:659–64.
8. McCullough JL, Hollier LH, Nugent M. Paraplegia after thoracic aortic occlusion: influence of cerebrospinal fluid drainage. J Vasc Surg 1988;7:153–60.
9. Lim KH, Connolly M, Rose D, Jacobowitz I, Cunningham JN. Prevention of reperfusion injury of the ischemic spinal cord: use of recombinant superoxide dismutase. Ann Thorac Surg 1986;42:282–6.
10. Kirshner DL, Kirshner RL, Heggeness LM, DeWeese JA. Spinal cord ischemia: an evaluation of pharmacologic agents in minimizing paraplegia after aortic occlusion. J Vasc Surg 1989;9:305–8.
11. Gerhardt EB, Stewart JR, Morrison JG, et al. Spinal cord protection during ischemia: comparison of mannitol, thiopental, and free radical scavengers. Surg Forum 1989;40:197–8.
12. Laschinger JC, Cunningham JN, Cooper MM, Krieger K, Nathan IM, Spencer FC. Prevention of ischemic spinal cord injury following aortic cross-clamping: use of corticosteroids. Ann Thorac Surg 1984;38:500–7.
13. Woloszyn TT, Marini CP, Coons MS, et al. Cerebrospinal fluid drainage and steroids provide better spinal cord protection during aortic cross-clamping than does either treatment alone. Ann Thorac Surg 1990;49:78–83.
14. Fowl RJ, Patterson RB, Gewirtz RJ, Anderson DK. Protection against postischemic spinal cord injury using a new 21-aminosteroid. J Surg Res 1990;48:597–600.
15. Yum SW, Faden AI. Comparison of the neuroprotective effects of the *N*-methyl-D aspartate antagonist MK-801 and the opiate receptor antagonist nalmafene in experimental spinal cord ischemia. Arch Neurol 1990;47:277–81.
16. Svensson LG, von Ritter CM, Groeneveld HT, et al. Cross-clamping of the thoracic aorta: influence of aortic shunts, laminectomy, papaverine, calcium channel blocker, allopurinol, and superoxide dismutase on spinal cord blood flow and paraplegia in baboons. Ann Surg 1986;204:38–47.
17. Svensson LG, Grum DF, Bednarski M, et al. Appraisal of cerebrospinal fluid alterations during aortic surgery with intrathecal papaverine administration and cerebrospinal fluid drainage. J Vasc Surg 1990;11:423–9.
18. Astrup J, Sorensen PM, Sorensen HR. Inhibition of cerebral oxygen and glucose consumption in the dog by hypothermia, pentobarbitol and lidocaine. Anesthesiology 1981;55:263–8.
19. Robertson CS, Foltz R, Grossman RG, Goodman JC. Protection against experimental ischemic spinal cord injury. J Neurosurg 1986;64:633–42.
20. Geddes IC, Quastel JH. Effects of local anesthetics on respiration of rat brain cortex in vitro. Anesthesiology 1956;17:666–71.
21. Haschke RH, Fink BR. Lidocaine effects on brain mitochondrial metabolism in vitro. Anesthesiology 1975;42:737–40.
22. Astrup J, Skovsted P, Gjerris F, Sorenson HR. Increase in extracellular potassium in the brain during circulatory arrest: effects of hypothermia, lidocaine, and thiopental. Anesthesiology 1981;55:256–62.
23. Evans DE, Catron PW, McDermott JJ, Thomas LB, Kobrine AI, Flynn ET. Effects of lidocaine after experimental cerebral ischemia induced by air embolism. J Neurosurg 1989;70:97–102.

Prevention of Arrhythmias After Noncardiac Thoracic Operations: Flecainide Versus Digoxin

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Cardiac arrhythmias are known complications of thoracic operations. The prophylactic value of flecainide administered as a constant-rate, intravenous infusion (0.15 mg $\cdot$ kg^{-1} $\cdot$ h^{-1}) after a loading dose (2 mg $\cdot$ kg^{-1}) was compared with digoxin (10 μg $\cdot$ kg^{-1} for 12 hours, then 0.25 mg $\cdot$ 24 h^{-1}) in a randomized study in 30 patients using Holter monitoring during the first 72 hours after operation. Drug monitoring was performed every day to keep a serum level of flecainide of 200 to 600 ng $\cdot$ mL^{-1} and a digoxin level of 0.8 to 2 ng $\cdot$ mL^{-1}. Failure, defined as the appearance of atrial fibrillation or flutter or the development of complex ventricular arrhythmias (Lown IVb and V), was observed in one patient in the flecainide group (7%) and in 7 patients in the digoxin group (47%) ($p < 0.05$). It is concluded that flecainide is more efficient than digoxin in preventing and treating cardiac arrhythmias after thoracic operations. At the dosage used side effects related to flecainide or digoxin were not observed.

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Ventricular and especially supraventricular cardiac arrhythmias are well known complications after thoracic operations [1, 2]. Digoxin has been extensively studied as a prophylactic antiarrhythmic drug in this clinical setting, but its value in this indication remains controversial [3]. The efficiency of flecainide, one of the newest type Ic antiarrhythmic drugs, in treating both ventricular and supraventricular arrhythmias has been demonstrated [4–6]. Recently flecainide in a placebo-controlled study has been shown to be very effective in reducing and preventing cardiac arrhythmias after noncardiac thoracic operations [7]. Therefore, our study was aimed at comparing the efficacy of flecainide and digoxin in preventing arrhythmias during the first 72 hours after a noncardiac thoracic operation. This period of monitoring was chosen because it had been reported that more than 60% of the arrhythmias appeared during the first 3 postoperative days [8].

Patients and Methods

Inclusion and Exclusion Criteria

Patients eligible for elective noncardiac thoracic operation were allowed to enter the study if they had no severe cardiac failure (stage III or IV according to the New York Heart Association classification), atrioventricular block (Mobitz type I or II, complete atrioventricular block), bifascicular block or bundle-branch block, sick sinus syndrome, unstable angina pectoris, history of myocardial infarction within 12 weeks of the start of the study, known allergy to flecainide or digoxin, or hepatic (aspartate aminotransferase or alanine aminotransferase level >3 times the normal values) or renal failure (plasma creatinine level >300 μmol/L) and were not taking antiarrhythmic drugs, digitalis, or calcium antagonists other than nifedipine. The study was approved by the ethics committee of our institution. Informed consent was obtained from all patients.

Study Design

Thirty consecutive patients meeting the inclusion criteria and without any exclusion criteria were randomly allocated in a single-blind fashion to one of two groups. Four patients were excluded: 3 were taking antiarrhythmic drugs and 1 was discovered to have complex ventricular arrhythmias during the preoperative Holter recording. Rhythm monitoring was performed with the Holter technique before and after operations during periods of from 24 up to 72 hours. Automatic and manual analysis of tapes was done without knowledge of the patients' condition.

Anesthetic management was similar for all patients: propofol was used for induction and maintenance of anesthesia, pancuronium for muscular relaxation, and fentanyl for analgesia. A central venous line (the tip of which was located at the carina by chest roentgenogram) and a femoral artery catheter were inserted in each patient. After admission to the surgical intensive care unit, group A patients received an infusion of flecainide (2 mg $\cdot$ kg^{-1}) during 60 minutes as a loading dose, followed by a maintenance infusion at a rate of 0.15 mg $\cdot$ kg^{-1} $\cdot$ h^{-1} up to the end of the study. Group B patients received an infusion of digoxin (10 μg $\cdot$ kg^{-1}, according to ideal body weight) during 12 hours, followed by a maintenance infusion of 0.25 mg $\cdot$ 24 h^{-1} up to the end of the study. Drug level monitoring was assessed every day and rate of perfusion was regulated to maintain a blood level of

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flecainide of 200 to 600 ng · mL^{-1} and a digoxin level of 0.8 to 2 ng · mL^{-1}.

Concurrent Treatment

Each patient had an epidural catheter inserted at the T3 to T4 level using the "loss of resistance" technique. Postoperative analgesia was provided by a continuous epidural infusion of fentanyl at a rate of 0.5 to 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$. When present, hypertensive episodes were treated either by nitrates, nifedipine, or phentolamine. Plasma potassium level was maintained between 3.6 and 4.5 mmol · L^{-1} by an intravenous infusion of potassium chloride. Plasma magnesium level was maintained between 0.8 and 1.15 mmol · L^{-1}. Supplement doses of magnesium chloride were given when necessary. It was possible to extubate the trachea of all patients at the end of the surgical procedure. Holter monitoring was started at the same time as the antiarrhythmic drug. Patients were questioned twice daily about the appearance of side effects.

Evaluation of the Results

Electrocardiographic monitoring was performed with a two-channel Marquette 8500 electronics recorder. Tapes were scanned on a marquette Laser-Holter monitor for detecting and quantitating supraventricular and ventricular arrhythmias. All tapes were also reviewed manually by one of the investigators (A.B.). Failure was defined as the appearance of one or more of the following dysrhythmias: (A) ventricular: complex ventricular arrhythmias graded according to Lown criteria (IVb = ventricular tachycardia; V = R on T phenomenon); (B) atrial: atrial fibrillation or flutter and paroxysmal supraventricular tachycardia. Episodes of paroxysmal supraventricular tachycardia were defined as an atrial rate greater than 140 beats · min^{-1} and a cycle length at least 15% faster than the basic sinus rhythm, with abrupt onset and termination and a P wave morphology distinctly different from sinus P wave; only episodes greater than 10 beats were considered. Any failure detected on the telemetric monitoring was changed to the protocol of the other group. However the appearance of serious ventricular arrhythmias in group A was treated by appropriate antiarrhythmic drug.

Flecainide level in serum was determined by high-pressure liquid chromatography with ultraviolet detection. Digoxin was determined by the activated *N*-acetylcysteine technique.

Statistical evaluation of the results was done using the Fisher exact test. Student's *t* test was used to compare demographic data. Results are given as mean ± standard error of the mean. A *p* value less than 0.05 was considered significant.

Results

Patients in groups A (flecainide; n = 15) and B (digoxin; n = 15) were similar for age, underlying pathologies, side of thoracotomy, and type of surgical procedures (Table 1).

Failure was observed in 1 patient in group A but in 7 patients in group B ($p < 0.05$; Table 2). In group A, atrial fibrillation developed in 1 patient on the third day and was not converted by digoxin; sinus rhythm was restored by electrical cardioversion on the fifth day. In group B, 3 patients had complex ventricular arrhythmias (Lown IV B). They appeared during the first day and were successfully treated by flecainide. Two patients had atrial fibrillation appearing during the second and third day. One of these arrhythmias was converted to sinus rhythm by flecainide; the other resolved spontaneously. The last two failures had episodes of paroxysmal supraventricular tachycardia, 1 of whom was successfully treated with flecainide, whereas tachyarrhythmia occurring in the other patient was detected only when analyzing the Holter recordings. Conversion of failures are summarized on Table 3.

Table 1. Distribution of Surgical Procedures

Type of Operation	Flecainide Group		Digoxin Group	
	Right	Left	Right	Left
Pneumonectomy	. . .	2	. . .	3
Lobectomy	4	5	6	1
Bilobectomy	1	. . .	1	. . .
Segmentectomy	1	. . .	1	. . .
Bisegmentectomy	. . .	. . .	. . .	1
Miscellaneous	1	1	. . .	2

Considering the effect of the side of the thoracotomy on the incidence of arrhythmias, no difference was observed between left and right thoracotomy in both groups.

The constant-rate flecainide infusion permitted us to maintain a serum concentration of flecainide between 200 and 600 ng · mL^{-1} during the whole course of the study; digoxin blood concentration was also maintained in the therapeutic range (Table 4).

Comment

This study showed a high incidence of severe arrhythmias (17%) according to the protocol criteria. Previous studies [8–10] have reported an incidence of dysrhythmias after noncardiac thoracic operations ranging from 3% to 40%, and developing mostly during the first 3 postoperative days [8]. Supraventricular tachydysrhythmias, atrial fibrillation in particular, were most often reported [8, 10]. Recently we found [7] using the Holter monitoring tech-

Table 2. Treatment Failure Distribution According to Treatment and Side of Thoracotomy

Variable	Flecainide Group			Digoxin Group		
	Right	Left	Total	Right	Left	Total
Number treated	7	8	15	8	7	15
Number of failures	0	1	1[a]	4	3	7

[a] $p < 0.05$.

Table 3. Conversion of Failures

Group	Number of Failures Treated	Drug Success
Flecainide	1	Digoxin, 0
Digoxin	5	Flecainide, 5

nique a very high incidence of complex ventricular arrhythmias in this clinical setting; a low incidence of premature ventricular contractions was only reported by Ghosh and Pakrashi [2]. The higher incidence of arrhythmias found in the present study is probably explained by differences in monitoring techniques among the previous study and our study. Holter monitoring is considered as the gold standard and is the only technique that permits a precise quantitation of the incidence of arrhythmias in patients requiring prolonged monitoring [11]. Indeed, Michelson and associates [11], comparing Holter and direct electrocardiographic monitoring in patients after cardiac operations, found much higher incidences of both supraventricular and ventricular arrhythmias with the former technique. In the present study 20% of failures were disclosed during analysis of tapes. The beneficial effect of flecainide as compared with digoxin not only in preventing but also in treating cardiac dysrhythmias was significant. Prevention of both atrial and ventricular arrhythmias was superior with flecainide. The successful treatment of failures from the digoxin group with flecainide was even more striking. The incidence of failures in the flecainide group (7%) is comparable with previous results (0%) [7]. The incidence of supraventricular dysrhythmias (27%) noted in the digoxin group compares also with the average of those previously reported [9, 10].

Thoracic operation is one of the procedures associated with the most severe postoperative pain and consequently most important activation of the neuroendocrine and metabolic response to stress [12]. In spite of the excellent quality of analgesia provided by epidural infusion of fentanyl, the sympathoadrenal response to stress is not blocked by epidural opiates [13] and the activation of the stress response is linked among other effects to arrhythmias, ventricular in particular [14]. Flecainide has been shown to be very efficacious in treating ventricular arrhythmias [15] and particularly those associated with a high level of catecholamines [16]. On the other hand, digoxin has little or no direct electrophysiological effects on the ventricle [17]. Beneficial effects of digoxin have been documented mainly in patients with moderate or severe heart failure resulting from left ventricular systolic dysfunction [18]. We noted that no episode of left ventricular failure supervened in the present study.

Table 4. Blood Drug Level[a]

Day	Flecainide (ng · mL^{-1})	Digoxin (ng · mL^{-1})
1	250 ± 31	1.15 ± 0.08
2	482 ± 49	1.25 ± 0.1
3	546 ± 45	1.20 ± 0.09

[a] Values are shown as mean ± standard error of the mean.

Experimental models have shown that atrial tachyarrhythmias may be due to abnormal impulse formation, reentry, or both. Reentry mechanism is the most likely explanation for atrial flutter and atrial fibrillation [19]. Clinical studies demonstrated that flecainide is very effective in the treatment of supraventricular tachyarrhythmias [20]. Right atrial effective period is significantly increased by infusion of flecainide [21]; digoxin, on the contrary, has no direct therapeutic effect on atrial refractoriness [17].

The protective effect of flecainide was afforded at serum concentrations in the middle of the previously reported therapeutic range [15, 22] and was not associated with any adverse effect. At the time of failure, blood drug levels of patients of both groups were in the therapeutic range.

Among the proposed mechanisms to explain atrial dysrhythmias (hypoxia, electrolyte or acid-base imbalance, vagal irritation), none have been convincing. Krowka and co-workers [23] found that tachydysrhythmias after pneumonectomy were associated with significant mortality within 30 days after the surgical procedure and occurred more frequently in patients in whom postoperative interstitial pulmonary edema or perihilar pulmonary edema developed. The suggestion that cardiac arrhythmias, supraventricular in particular, are associated with volume–pressure-induced problems deserves further study. In an animal model, Zeldin and associates [24] demonstrated that dogs with postpneumonectomy pulmonary edema had higher pulmonary pressures; pulmonary hypertension is also associated with an increased perioperative mortality after orthotopic heart transplantation [25].

As tachydysrhythmias after pneumonectomy were recently shown to be associated with significant mortality [23], the efficacy of flecainide in preventing and treating them has clear clinical relevance; however, the effect of prevention of arrhythmias in decreasing the morbidity and mortality rates was not addressed by our study and remains to be evaluated. Moreover, definition of the precise mechanisms leading to cardiac arrhythmias in this clinical setting warrants further studies.

In conclusion, a constant-rate, intravenous infusion of flecainide administered during the first 3 days after thoracotomy was superior to digoxin in preventing and treating tachyarrhythmia; at the dosage used side effects related to flecainide were not observed.

We wish to thank Drs Grandjean and Etienne, the nurses of the intensive care of Montreux and Fribourg for their collaboration and assistance, and Holtmed Scanning services SA Lausanne for the automatic tape analysis.

References

1. Currens JH, White PD, Churchill ED. Cardiac arrhythmias following thoracic surgery. N Engl J Med 1943;229:360–4.
2. Ghosh P, Pakrashi C. Cardiac dysrhythmias after thoracotomy. Br Heart J 1972;34:374–6.
3. Juler GL, Stemmer EA, Connolly JE. Complications of prophylactic digitalization in thoracic surgical patients. J Thorac Cardiovasc Surg 1969;58:352–60.
4. Goy JJ, Grbic M, Hurni M, et al. Conversion of supraventricular arrhythmias to sinus rhythm using flecainide. Eur Heart J 1986;6:518–24.

5. Roden DM, Woosley RL. Flecainide. N Engl J Med 1986;315:36–41.
6. Borgeat A, Goy JJ, Maendly R, Kaufman U, Grbic M, Sigwart U. Flecainide versus quinidine for conversion of atrial fibrillation to sinus rhythm. Am J Cardiol 1985;58:496–8.
7. Borgeat A, Biollaz J, Bayer-Berger M, Kappenberger L, Chapuis G, Chiolero R. Prevention of arrhythmias by flecainide after noncardiac thoracic surgery. Ann Thorac Surg 1989;48:232–4.
8. Mowry F, Reynolds EF. Cardiac rhythm disturbances complicating resectional surgery of the lung. Ann Intern Med 1964;61:688–95.
9. Shields TW, Yjiki GT. Digitalization for prevention of arrhythmias following pulmonary surgery. Surg Gynecol Obstet 1968;126:743–6.
10. Wheat MW, Burford TH. Digitalis in surgery: extension of classical indications. J Thorac Cardiovasc Surg 1961;41:162–8.
11. Michelson EL, Morganroth J, Mac Vaug H. Postoperative arrhythmias after coronary artery and cardiac valvular surgery detected by longterm electrocardiographic monitoring. Am Heart J 1979;97:442–8.
12. Kehlet H. Pain relief and modification of the stress response. In: Cousins MJ, Phillips GD, ed. Acute pain management. 1st ed. Edinburgh: Churchill Livingstone, 1986:49.
13. Kehlet H. The modifying effect of general and regional anesthesia on the endocrine-metabolic response to surgery. Regional Anesth 1982;7:S38–48.
14. Reiz S, Balfors E, Sorensen MB, Häggmark S, Nyhman H. Coronary hemodynamic effects of general anesthesia and surgery: modification by epidural analgesia in patients with ischemic heart disease. Regional Anesth 1982;7(Suppl):S9–18.
15. Holmes B, Heel RC. Flecainide: a preliminary review of its pharmacodynamic properties and therapeutic efficacy. Drugs 1985;29:1–33.
16. Dobmeyer D, Muir WW, Schaal SF. Antiarrhythmic effects of flecainide against canine ventricular arrhythmias induced by two-stage coronary ligation and halothane-epinephrine. J Cardiovasc Pharmacol 1985;7:238–44.
17. Atlee JL III. Drugs used for the treatment of cardiac dysrhythmias. In: Atlee JL, ed. Perioperative cardiac dysrhythmias: mechanisms, recognition, management. 1st ed. Chicago: Year Book Medical Publishers, 1985:272.
18. Lewis RP. Digitalis: a drug that refuses to die. Crit Care Med 1990;18:S5–14.
19. Benditt DG, Benson DW, Dunnigan A, Gornick CC, Anderson RW. Atrial flutter, atrial fibrillation and other primary atrial tachycardias. Med Clin N Am 1984;68:895–918.
20. Crozier IG, Ikram H, Kenealy M, Levy L. Flecainide acetate for conversion of acute supraventricular tachyarrhythmias to sinus rhythm. Am J Cardiol 1987;59:607–9.
21. Camm JA, Hellestrand KH, Nathan AW, Bexton RS. Clinical usefulness of flecainide acetate in the treatment of paroxysmal supraventricular arrhythmias. Drugs 1985;29(Suppl 4):7–13.
22. Conard GJ, Cronheim GF, Klempt HW. Relationship between plasma concentrations and suppression of extrasystole by flecainide acetate (R-818), a new antiarrhythmic, in patients. Drug Res 1982;32:155–9.
23. Krowka MJ, Pairolero PC, Trastek VF, et al. Cardiac dysrhythmias following pneumonectomy. Clinical correlates and prognostic significance. Chest 1987;91:490–5.
24. Zeldin RA, Normandin D, Landtwing D, Peters RM. Postpneumonectomy pulmonary edema. J Thorac Cardiovasc Surg 1984;87:359–65.
25. Kawaguchi A, Gandjbakhch I, Pavie A, et al. Factors affecting survival after heterotopic heart transplantation. J Thorac Cardiovasc Surg 1989;98:928–34.

INVITED COMMENTARY

Dr Borgeat and associates report the results of a prospective, controlled trial comparing prophylactic treatment of cardiac arrhythmias after thoracic operations with either digoxin or flecainide. Flecainide was very effective in preventing atrial and ventricular arrhythmias. Digoxin was relatively ineffective and, citing other work, Borgeat and associates conclude digoxin was not superior to placebo. There were apparently no episodes of sustained ventricular tachycardia or ventricular fibrillation, and the degree of hemodynamic compromise in response to sustained atrial arrhythmias was not reported.

The Cardiac Arrhythmia Suppression Trial examined the hypothesis that prophylactic treatment of ventricular ectopy in the postmyocardial infarction population would improve survival. Despite impressive efficacy in reducing the frequency of ectopy, at 10 months of follow-up the flecainide group had more than twice the *mortality* of the placebo group (5.1% versus 2.3%) [1]. The package insert for Tambocor (flecainide) quotes proarrhythmia rates of 13% to 26% in patients with previous sustained ventricular arrhythmias, with 10% of those treated with a higher dose having proarrhythmia that resulted in death [2].

In considering whether to prophylactically treat arrhythmias, the endpoint should be carefully considered. Atrial fibrillation, atrial flutter, and multifocal atrial tachycardia can be associated with a rapid ventricular response and hemodynamic collapse. Beta blockers and calcium blockers may be of use and, with digoxin, may control the ventricular response. Sustained ventricular tachycardia and ventricular fibrillation are disastrous and, if primary prophylaxis is believed to be indicated, lidocaine has been shown to be of benefit in an acute myocardial infarction [3], although this may not apply to other settings.

Isolated ventricular premature depolarizations, infrequent short runs of nonsustained ventricular tachycardia, and R on T depolarizations do not cause hemodynamic compromise; in and of themselves, these extra beats do not require treatment. Currently, there is no study showing that treatment of these ventricular arrhythmias improves prognosis. In the absence of data demonstrating improvement in morbidity or mortality, in light of the CAST results, and considering the possible proarrhythmic effects of all antiarrhythmic drugs, including flecainide, one should carefully question whether these arrhythmias should be treated.

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References

1. The cardiac arrhythmia suppression trial (CAST) investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after acute myocardial infarction. N Engl J Med 1989;321:406–12.
2. Tambocor product literature. Physicians Desk Reference. Oradell, NJ: Medical Economics Co, 1990.
3. Lie KI, Wellens HJ, Van Capelli FJ. Lidocaine in the prevention of primary ventricular fibrillation. A double-blind randomized study of 212 consecutive patients. N Engl J Med 1974;291:1324.

REVIEW OF RECENT BOOKS

Wanderjahr: The Education of a Surgeon, Edward D. Churchill

Edited and annotated by J. Gordon Scannell, MD
Boston, MA, The Francis A. Countway Library of Medicine, 1990
213 pp, illustrated, $18.95

Reviewed by Thomas B. Ferguson, MD

This delightful little volume has been 64 years in preparation, but is certainly worth the wait.

As was (and still is) the custom at Harvard Medical School, young faculty members of unusual promise were offered a Travelling Fellowship—the Moseley—for a year of broadening and seasoning. Dean David Edsall proffered the Moseley to Edward D. Churchill for the academic year 1926 to 1927, 2 years after Churchill had completed his surgical residency. Dr Churchill took full advantage of this windfall, visiting clinics and observing surgeons all over Europe. His impressions of the people—Sauerbruch, Brauer, Max Borst (Hans Borst's father), Leriche, and Jacobaeus—and the places—England, Germany, Switzerland, and Scandinavia, to name a few—construct a fascinating mosaic of the period. But the year was not all work; there was time for skiing, sightseeing, and astute observation of the social scene, the latter particularly apt in light of the major role he would later play in World War II. He even had time to woo and win Mary Barton, his lovely wife of 45 years, with the lure of a ceremony in rural Kent and a honeymoon on the continent.

During the year, which he later referred to as his Wanderjahr, Churchill took extensive notes, but never published them. In 1955 he was persuaded to sit for a series of interviews with oral historian Saul Benison. The Wanderjahr was recorded, reflected upon, and evaluated in the light of the busy 28 intervening years. The transcripts remained among his unpublished papers until they came to the attention of Dr J. Gordon Scannell, pupil and close friend of Dr Churchill, and eminent thoracic surgeon and scholar in his own right. Dr Scannell is editor of the *Harvard Medical Alumni Bulletin*.

The body of the book is Churchill's log, certainly leavened by thoughts and ideas added later. There is a foreword by Benison, telling how the tapes came to be, and a preface, introduction, and epilogue by Dr Scannell that nicely set the Wanderjahr in context and emphasize how pivotal this time was in molding the career of this remarkable man. An inspired addition to the volume is what Dr Scannell terms the Biographical Register—short, lucid entries about every physician named in the text.

Only 213 pages in length, this book has a nugget for everyone. For the history buff, it is a fascinating tale. For the silver fox thoracic surgeons, there is a stroll and a handshake with many of the first-generation greats. And for the young up-and-comers, it affirms the importance of a Wanderjahr in one's life, and provides a journey with a role model without peer.

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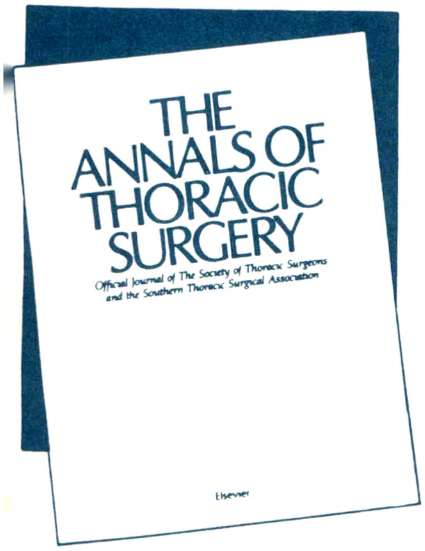
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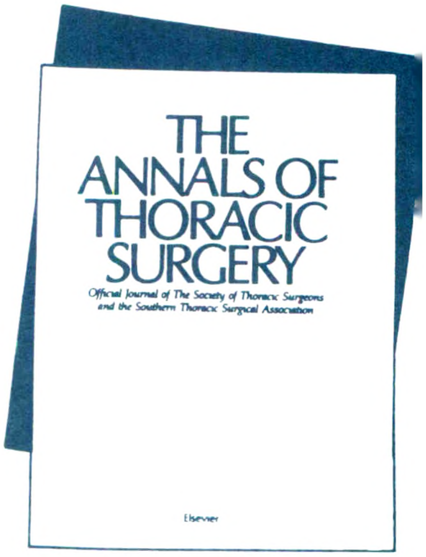
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Hypertrophy of Nodules of Arantius and Aortic Insufficiency: Pathophysiology and Repair

Nadiv Shapira, MD, Javier Fernandez, MD, Kathleen W. McNicholas, MD,
A. Jorge Serra, MD, Kathryn Hirschfeld, RN, Paschal M. Spagna, MD,
and Gerald M. Lemole, MD

Medical Center of Delaware, Wilmington, Delaware

Aortic insufficiency (AI) due to fibrosis and thickening of the nodules of Arantius in the otherwise normal aortic valve was found in 11 adults (age range, 41 to 65 years) between 1976 and 1988. Nine had concomitant mitral stenosis; 2 had coronary artery disease. In 6 patients AI was graded 3+ or greater; in 5 it was less than 3+. Correction of AI and restoration of cuspid flexibility and apposition by shaving the hypertrophied nodules was accomplished in all, with postrepair AI graded as 1+ or less. There was one hospital death, a patient who had prior mitral operation. Mean follow-up was 68 ± 56 months. Only 1 patient had late (6 years) recurrent serious (3+) AI. Nine continued to have 1+ or less AI, based on echocardiography or catheterization (n = 6) or on physical examination performed at a mean of 74 months. We conclude that thickening of the nodules of Arantius may cause AI. Long-term correction can be accomplished by sculpturing of the involved cusps.

(Ann Thorac Surg 1991;51:969–72)

Aortic valvar insufficiency (AI) results from either annular dilatation, abnormal aortic cusps, or both [1–3]. The pathological processes involving the cusps known to cause AI include retraction, prolapse, perforation, and destruction [1–3]. We have recognized another cuspid pathological feature, the abnormal thickening, enlargement, and stiffening of the central segment of the closure line of the cusps, the nodules of Arantius, as a cause for AI. Correction of AI in these valves did not require valve replacement, and the flexibility and coaptation of their cusps could be restored simply by shaving of these protuberances. This report describes this entity and the repair, as well as the early and late results.

Patients and Methods

Between 1976 and 1988, correction of AI by valve sculpturing was accomplished in 11 adult patients, 7 women and 4 men, with a mean age of 54 ± 6 (standard deviation) years (range, 41 to 65 years). All had trileaflet aortic valves without annular dilatation, and all were nonstenotic or only mildly stenotic. Nine patients had a history of rheumatic heart disease, and AI was associated with advanced mitral stenosis with a mean mitral valve gradient and area of 14.1 ± 4.4 mm Hg and 0.76 ± 0.19 cm^2, respectively. The AI in 5 of these patients was graded as 3+ and was considered serious, and in 4 it was 2+ or less. Two of them had a mild aortic valve gradient (10 and 25 mm Hg), one had serious coronary artery disease, and 2 had mitral commissurotomy at an earlier date. Two patients had no history of rheumatic heart disease. One of them had serious coronary artery disease and 4+ AI, and the other had ascending aortic aneurysm and 2+/3+ AI. Altogether, in 6 patients aortic insufficiency was serious and was part of the primary indication for operation, whereas in 5 it was only a secondary objective.

Operative Procedure

Cardiopulmonary bypass with moderate systemic hypothermia was employed in all cases. Myocardial protection was achieved by direct coronary perfusion until 1979 and by cardioplegic arrest thereafter. A left ventricular vent was inserted in all patients. Criteria employed to establish that the mechanism of AI was due to hypertrophy of the nodules of Arantius were observational and included (1) absence of annular dilatation and (2) normal condition of all cusps except for the presence of stiff and hypertrophied fibrous nodules located at their lines of apposition, which prevented adequate coaptation (Fig 1a). The hypertrophied tissue, which is located at the ventricular aspect of the cusps, was shaved using a No. 11 scalpel blade applied tangentially to the surface of the cusps (Fig 1b). One or two traction sutures passed through these hypertrophied areas were helpful in lining them up and sculpturing the cusps precisely to the appropriate thickness. Repair was considered to be satisfactory if complete apposition of all three cusps was accomplished and the center points of the three cusps reached each other without tension (Fig 1c). Repair of the aortic valve per se was not an indication for anticoagulation. Approximate time of valve sculpturing was 10 minutes.

Follow-up

Follow-up was obtained from office or telephone interviews or from referring physicians and in most cases included heart catheterization (n = 6) or two-dimensional Doppler echocardiography (n = 4). End points of fol-

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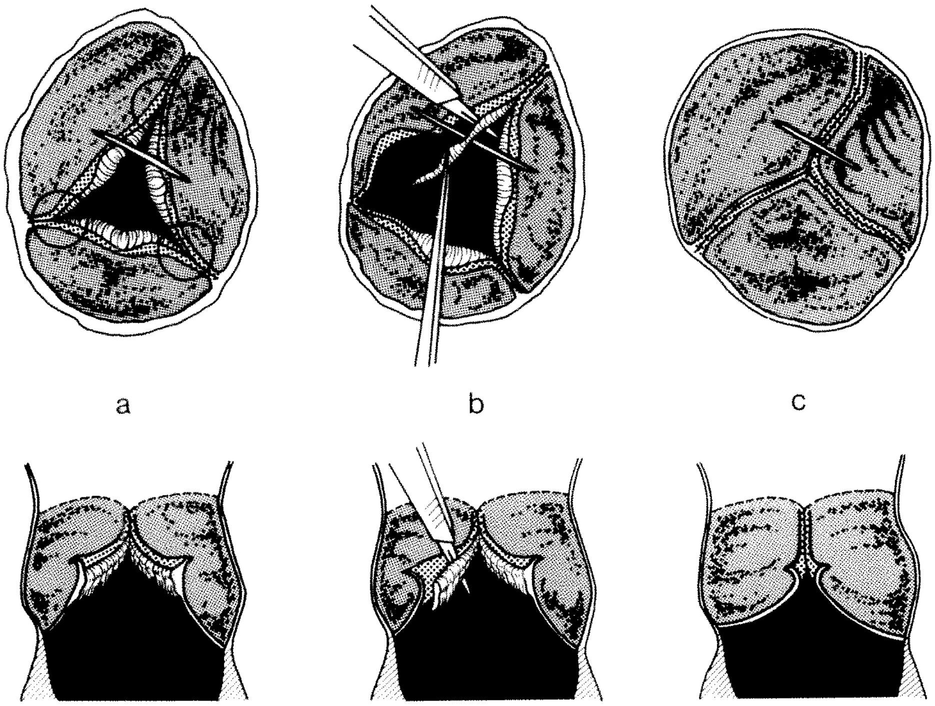

Fig 1. Aerial view (top panels) of the aortic valve, showing lack of cuspid coaptation at the center of the valve due to enlarged nodules of Arantius (a). The circles *indicate the points where proper apposition is prevented by the nodules. By shaving the enlarged nodules (b), normal apposition of all three cusps is restored (c). Views of cross-sections at the marker lines are depicted in the lower panels.*

low-up were death or aortic valve replacement. Values are expressed as mean ± standard deviation.

Results

All aortic valves were repaired by cuspid sculpturing. One patient had commissurotomy as well. Appropriate coaptation was restored in all, with trivial or no residual AI. None required aortic valve replacement. Nine patients had a concomitant mitral commissurotomy, 2 had coronary artery bypass, and 1 had ascending aortic aneurysm repair. One patient who had a prior mitral valve repair died due to excessive bleeding and cardiac failure. The shaved tissue was available for histopathological examination in 8 patients and revealed homogeneous dense fibrous tissue in excess of what is observed in valves free of AI (Fig 2).

Mean follow-up was 68 ± 56 months (range, 5 to 156 months) (Fig 3). One patient had late recurrent AI; a patient who was initially operated on for 4+ AI and coronary artery disease had development of 3+ AI and serious mitral stenosis and insufficiency 6 years later and underwent aortic and mitral valve replacements. Nine patients had no recurrent or only trivial AI. Mitral valve restenosis requiring mitral valve replacement developed in 4 of them, but in 2, the surgeon elected to replace the aortic valve although it functioned well. The other 5 have never been reoperated on; 1 of them died suddenly 6 months after repair while in New York Heart Association class I, and 4 remained well and alive at 5, 6, 120, and 156 months after repair.

Comment

After intraoperative evaluation of many incompetent aortic valves, it was realized that in some, the mechanism of insufficiency could not be ascribed to one of the known categories of annular dilatation or cuspid retraction, prolapse, perforation, or retraction [1–3], but was rather due to cuspid malcoaptation secondary to stiffening of their line of apposition by enlarged nodules of Arantius. The nodules of Arantius are small congregations of fibrous tissue located at the anatomical midpoint of each aortic cusp, at or close to its free edge [1, 3] (Fig 4). Collagenous ridges extend from both sides of the nodules toward the commissures, where they blend with the aortic wall and form the lines of closure or apposition of the cusp [1, 3]. When a competent valve closes, the nodules of the three cusps meet at the center. Coaptation of the entire length of the lines of apposition and the cusp tissue above them (lunulae) against each other makes the valve competent.

Some degree of hypertrophy of the nodules is seen frequently, particularly in elderly patients [1], but usually it does not prevent proper cuspid coaptation. When the hypertrophy is excessive and extends on either side of the nodules along the lines of apposition and involves a considerable portion of these lines, it may make them stiff like rigid bars. As a result, these otherwise normal cusps can abut each other only at the periphery while the center of the valve stays opened like a triangle bordered by these three bars (see Fig 1). By shaving of these exuberant nodules, these otherwise normal cusps can regain their flexibility and full coaptation. The successful abolishment of AI in the 11 patients reported here supports the aforementioned theory of this unique pathophysiology.

Thickening of the free edge of the cusps has been described in association with aortic root dilatation [1–3] and considered to be secondary to, rather than causative of, AI. The abnormal thickening in the entity described in this report did not involve the free edge of the cusps, none of the involved patients had annular dilatation, and correction of AI did not include procedures aimed toward diminishing annular dimensions.

The majority of the patients in this series have had a history of rheumatic heart disease. Postinflammatory AI has been characterized by diffuse fibrosis and scarring extending from the cuspid lines of insertion, retracting the cusps [1, 2] and resulting in a reduction in cuspal area. The condition described in this report may represent a variant from that typically found in the postrheumatic aortic valve, in which the early inflammation and the subsequent fibrosis is confined only to the lines of apposition while sparing the rest of the cusps. We speculate that because the movement at the tip of the cusps during the cardiac cycle is maximal, the nodules of Arantius and the lines of apposition just next to them are subjected to the maximal mechanical impact during valve closure. When associated with inflammatory changes, this impact may subsequently result in hypertrophy limited to these areas. The reason why in some patients the inflammatory changes are confined to the lines of apposition requires further clinical and pathological investigation.

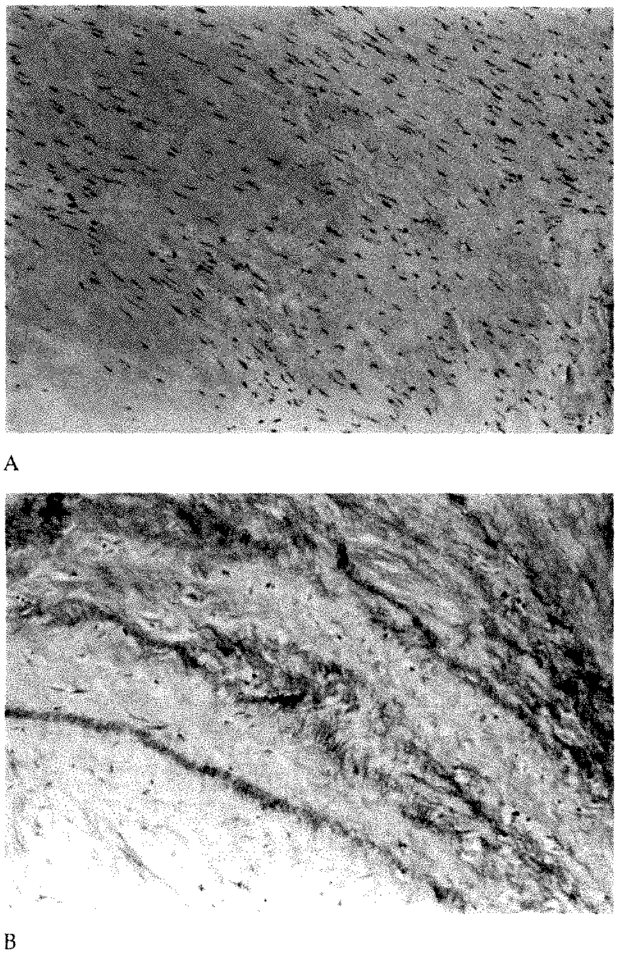

Fig 2. High-power view of a section across hypertrophied nodules of Arantius, demonstrating dense homogeneous fibrosis (A; hematoxylin and eosin, ×40 before 50% reduction), which can disrupt the elastica (B; elastic stain, ×40 before 50% reduction).

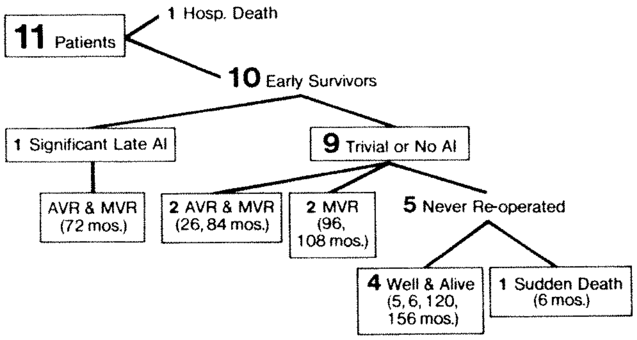

Fig 3. Schematic profile of the patients who have undergone aortic valve sculpturing. (AI = aortic insufficiency; AVR = aortic valve replacement; MVR = mitral valve replacement.)

The fact that during a mean follow-up of 68 months, only 1 (10%) of the patients had development of recurrent (late) AI suggests that the repair is long-lasting and may even provide a cure for patients with this entity. Considering that 27% to 46% of patients with AI have a history of rheumatic heart disease [2, 3], and based on our impression that not more than 10% of patients with rheumatic AI have disease amenable to cuspal sculpturing, it is reasonable to assume that the procedure could be applied to fewer than 5% of patients with AI. For patients with serious AI who are candidates for aortic valve replacement, considering the 3% to 5% annual rate of major prosthetic aortic valve–related complications [4–6], retaining rather than replacing their native valves can be highly rewarding. For patients with nonserious AI undergoing operation for other cardiac problems, because AI can be tolerated over many years [7], the merits of sculpturing the valves, although simple, can be judged only by analysis of the effect of the procedure on the natural history of the disease. However, AI that is considered to be insignificant under normal circumstances may present a serious problem for patients with compromised left ventricular function during their recovery from a cardiac operation, particularly if insertion of an intraaortic balloon

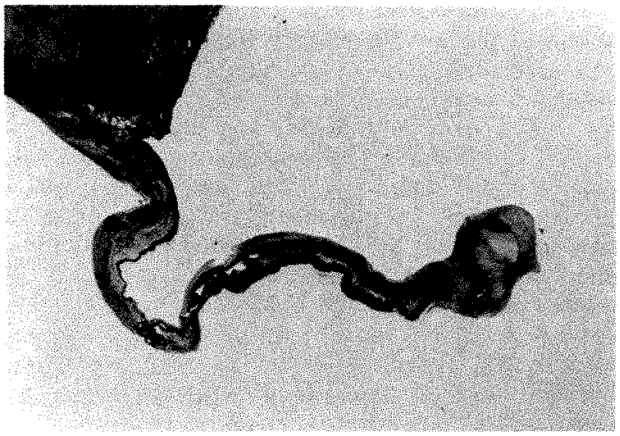

Fig 4. A histological cross section of a cusp removed from a patient with a normal aortic valve. A normal-sized nodule of Arantius is seen. (Hematoxylin and eosin, ×20 before 50% reduction.)

pump is required. Correction of AI by cuspal sculpturing may offer them a simple solution.

We acknowledge the contributions of Jacquelynn M. Wilson and Karen C. McFadden for their editorial assisting and preparation of the manuscript.

References

1. Davies MJ, Path FRC. The aortic valve. In: Davies MJ, Path FRC. Pathology of cardiac valves. London-Boston: Butterworths & Co, 1980:1–61.
2. Olson LJ, Subramanian MB, Edwards WD. Surgical pathology of pure aortic insufficiency: a study of 225 cases. Mayo Clin Proc 1984;59:835–41.
3. Guiney TE, Davies MJ, Parker DJ, Leech GJ, Leatham A. The aetiology and course of isolated severe aortic regurgitation: a clinical, pathological, and echocardiographic study. Br Heart J 1987;58:358–68.
4. Rahimtoola SH. Outcome of aortic valve surgery. Circulation 1979;60:1191–5.
5. Dale J, Levang O, Eng I. Long term results after aortic valve replacement with four different prosthesis. Am Heart J 1980; 99:155–61.
6. Cohn LH, Allred EN, DiSesa VJ, Sawtelle K, Shemin RJ, Collins JJ. Early and late risk of aortic valve replacement. A 12 year concomitant comparison of the porcine bioprosthetic and tilting disc prosthetic aortic valves. J Thorac Surg 1984;84: 695–705.
7. Bonow RO, Rosing DR, McIntosh GL, et al. The natural history of asymptomatic patients with aortic regurgitation and normal left ventricular function. Circulation 1983;3:509–17.

INVITED COMMENTARY

Dr Shapira and colleagues bring to light several points worth discussing at a time when the success of mitral valve repair seems to have rekindled an interest in aortic conservation. Although they only report 11 cases of aortic valve repair, their report is a reminder that not every regurgitant lesion must necessarily be treated by valve replacement. It also emphasizes that this conservative attitude requires a detailed analysis of the lesions encountered and their relative value in the genesis of the regurgitation.

They describe a pathological finding that my colleagues and I have seen very often in the young rheumatic patient. In the presence of otherwise normal looking cusps, the free edge is considerably thickened along its entire length, being maximal at the center and thinning out toward the commissural end. The visual impression, at least in the young patient, is of a free edge that has "rolled in" toward each sinus of Valsalva, resulting in a central lack of coaptation. We have seen this lesion in rheumatic patients, usually operated on for mitral disease, with an associated moderate aortic regurgitation and often concomitant mild stenosis. It is conceivable that in the older patient, as reported by Shapira and colleagues and seen by ourselves, this free edge thickening develops into a discrete fibrous band. The suggested term of *hypertrophy of the nodules of Arantius* is probably inappropriate as anatomically the nodule only constitutes the midpoint of each free edge. A *lunulae fibrosis* might be a better alternative given that the normal lunulae or leaflet contact areas extend along the free edge and thin out as they reach the commissures.

The proposed surgical treatment was apparently successful even if only used in a few patients. Our approach, started in 1974 [1] and applied in more than 100 patients, has been different in as much as an attempt was undertaken to unroll the free edge by multiple small incisions made on the sinus and lower aspect of the thickening followed by gentle traction. Very often a surprising increase in the total cusp area could be achieved. In older patients in whom the fibrosis has progressed to a more solid bar, its excision improves cusp mobility. We have also used this "shaving" technique in thickened cusps, but usually close to the fused commissures after their splitting.

It is surprising, however, that in the author's experience this single maneuver was sufficient to restore competence, whereas in ours all patients also underwent a subcommissural annuloplasty as originally described by Cabrol and associates [2].

The satisfactory long-term results described by Shapira and colleagues coincide with our reported experience [3] and emphasize the similarities in conservative operation on all cardiac valves. This operation requires a detailed analysis of the lesions, a variety of surgical maneuvers, and reliable intraoperative testing methods. The danger of early reoperation for residual regurgitation is always present. The determinant factor for conservation is, however, the mental attitude of the surgeon who, although cautious to convert, becomes enthusiastic once the superior long-term results become apparent. The present report contributes toward that goal.

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References

1. Duran CMG. Reconstructive techniques for rheumatic aortic valve disease. J Cardiac Surg 1988;3:23–8.
2. Cabrol C, Guiraudon G, Bertrand M. Le traitement de l'insuffisance aortique par l'annuloplastie aortique. Arch Mal Coeur 1966;59:1305–12.
3. Duran CMG, Alonso J, Gaite L, et al. Long term results of conservative repair of the rheumatic aortic valve insufficiency. Eur J Cardio-Thorac Surg 1988;2:217–23.

Neodymium:Yttrium-Aluminum Garnet Laser–Assisted Pulmonary Resections

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The neodymium:yttrium-aluminum garnet laser is a new approach to limited pulmonary resection. It avoids distortion of surrounding pulmonary tissue and potential pleural space problems, which can occur with mechanical stapler resections. We have recently used this laser to manage 39 pulmonary lesions in 20 patients. There were no major postoperative complications, and air leak after resection was minimal. Neodymium:yttrium-aluminum garnet laser excision is a useful method that may have an advantage over mechanical stapling techniques for the limited resection of many pulmonary lesions.

(Ann Thorac Surg 1991;51:973–8)

The neodymium:yttrium-aluminum garnet (Nd:YAG) laser is a powerful and precise tool that has proven efficacy in the endoscopic management of benign and malignant tracheobronchial lesions [1, 2]. Recent reports [3, 4] have documented the efficacy of the Nd:YAG laser in sealing microscopic pulmonary vessels, bronchioles, and lymphatics during open thoracic surgical procedures. We review here our clinical experience with use of the Nd:YAG laser in the limited resection of 39 pulmonary lesions in 20 recent patients.

Material and Methods

Patient Population

Over the last 14 months, 20 patients diagnosed as having new solitary or multiple pulmonary parenchymal lesions (n = 39) were selected for Nd:YAG laser pulmonary parenchyma–sparing resections (Table 1). Nine women and 11 men with a mean age of 63 years made up the study population. Pulmonary function was assessed in all patients preoperatively and at 1 month after operation.

Neodymium:yttrium-aluminum garnet laser resection was used for the diagnosis and primary management of the pulmonary lesions in 18 of the 20 patients. In 2 patients with a diagnosis of bronchogenic carcinoma, completion lobectomy was chosen after laser resection when positive interlobar lymph nodes were identified during intraoperative staging of the cancer. One patient underwent, through a median sternotomy approach, a combined left pneumonectomy to manage a squamous cell carcinoma involving the left pulmonary hilum and laser-assisted wedge resection of a contralateral synchronous adenocarcinoma in the right upper lobe (Fig 1).

The pathological diagnosis of the lesions resected by the laser approach alone was varied. Segmental resection encompassing a 1.0-cm margin about the lesion combined with interlobar and mediastinal lymphadenectomy was used as the sole management for 2 patients with marginal pulmonary function found to have stage I bronchogenic carcinoma. Two patients found to have pulmonary nodules consistent with implantation of metastatic carcinoma also underwent laser resection alone. Seven patients underwent solitary or multiple resection of pulmonary nodules ultimately diagnosed as granulomas. Two patients with giant apical bullous disease required Nd:YAG laser ablation of pathological air spaces, which had resulted in a persistent large bronchopleural fistula and pulmonary collapse despite tube thoracostomy in 1 patient. The nature of the lesions resected in 6 other patients are identified in Table 1.

Use of the Nd:YAG laser enabled a limited resection of 11 deep-seated lesions that would otherwise have required lobectomy for safe removal (Fig 2). Three of these resections were along anatomical segmental planes; all the other deep Nd:YAG–laser resections crossed anatomical segmental districts. Attempting stapled resection of these deep lesions could have resulted in substantial pulmonary distortion leading to impairment of the local circulation, loss of function of the surrounding lung tissue, and possible pleural space problems [5, 6].

The intraoperative blood loss, total operative time, postoperative hospital stay, and duration of chest tube requirements were recorded. The total energy delivered to the pulmonary parenchyma during the resection was documented. All major postoperative morbidity was noted.

Operative Technique

A 100-W SLT Nd:YAG unit (Surgical Laser Technologies, Malvern, PA) was used to deliver 30 to 40 W of continuous-wave energy for the pulmonary resections. All windows to the operative suite were blocked, and operating room personnel wore protective eyewear to guard against the 1,060-nm wavelength of the Nd:YAG laser.

Several thoracic incisional approaches were selected for

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Table 1. Lesions Resected with Neodymium:Yttrium-Aluminum Garnet Laser

Type of Lesion	No. of Lesions
Primary cancers	6
Squamous cell	1
Adenocarcinoma	5
Metastatic cancers	6
Bladder	3
Colon	3
Benign lesions	27
Hamartoma	2
Granuloma	17
Pseudoxanthoma	1
Hemorrhagic cyst	3
Giant bullae	2
Amyloid nodule	1
Lung scar	1
Total	39

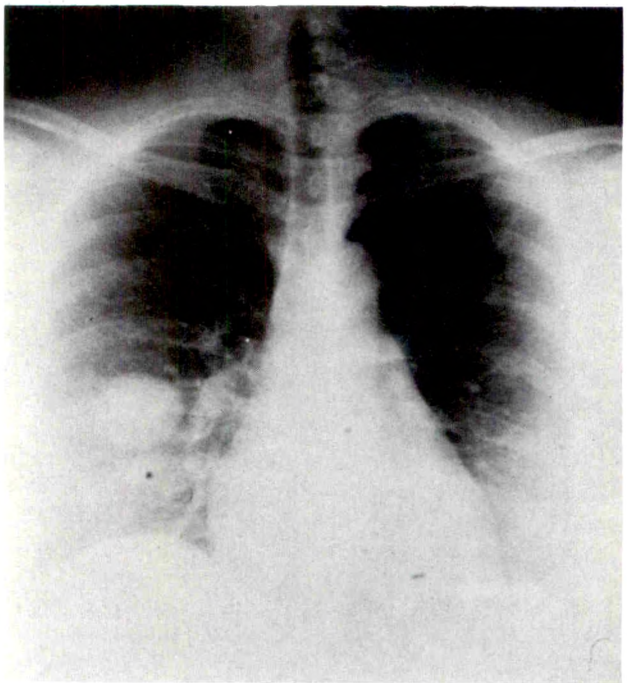

Fig 2. Posteroanterior chest roentgenogram revealing a right lower lobe nodule 4 cm in diameter. Resection with the neodymium:yttrium-aluminum garnet laser avoided the need for lobectomy for this benign granuloma.

the laser resections. A muscle-sparing lateral thoracotomy was used in 10 patients. Resection was accomplished through a limited axillary thoracotomy on three occasions. Bilateral pulmonary nodules were resected in 2 patients through a median sternotomy. The remaining five resections were performed through a standard posterolateral thoracotomy.

A double-lumen endotracheal tube or bronchus-blocking catheter was routinely used to obtain collapse of the involved lung during the laser resection. Once total atelectasis was achieved, the lesion to be resected was brought into view by placing moist laparotomy packs behind the involved lobe of the lung. The Nd:YAG laser beam was activated, the free Nd:YAG fiber hand-held, and the beam then positioned approximately 2 cm from the visceral pleura over the lesion. For superficially located lesions, the laser incision was fashioned to encircle a 1-cm visceral pleural margin about the lesion (Fig 3). A nonanatomical segmental plane was established, and excavation of the mass was accomplished by gentle traction to allow demarcation between the lesion and the surrounding uninvolved lung tissue.

As the dissection progressed, it was important to vary the laser-beam spot size used to achieve the desired tissue effects of the Nd:YAG laser. Reducing the spot size by moving the laser fiber closer to the tissue increased the power density, which facilitated vaporization of the pulmonary parenchyma [7, 8]. Defocusing the beam allowed greater coagulative effects from the laser to occur (Fig 4). Use of this technique permitted a more rapid resection with effective hemostasis and control of potential air leaks from the raw pulmonary parenchymal surface. Periodic palpation of the mass assured complete excision of the nodule and assisted in maintaining a margin of resection several millimeters wide about the mass.

For nonanatomical resection of deeper-seated lesions, the lung parenchyma was incised down to the lesion before a circumscribing plane of dissection was developed about the mass (Fig 5). We emphasize that careful attention to the segmental bronchopulmonary anatomy is essential during the dissection to avoid injury to the surrounding, potentially "spared" lung parenchyma [9, 10]. Inadvertent injury to the uninvolved segmental pul-

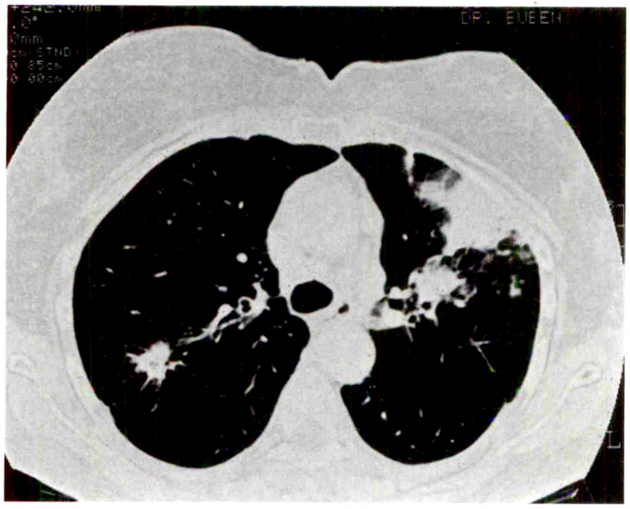

Fig 1. Computed tomographic scan of a patient with bilateral synchronous pulmonary malignancies who was managed with left pneumonectomy and neodymium:yttrium-aluminum-garnet laser resection of the right upper lobe lesion.

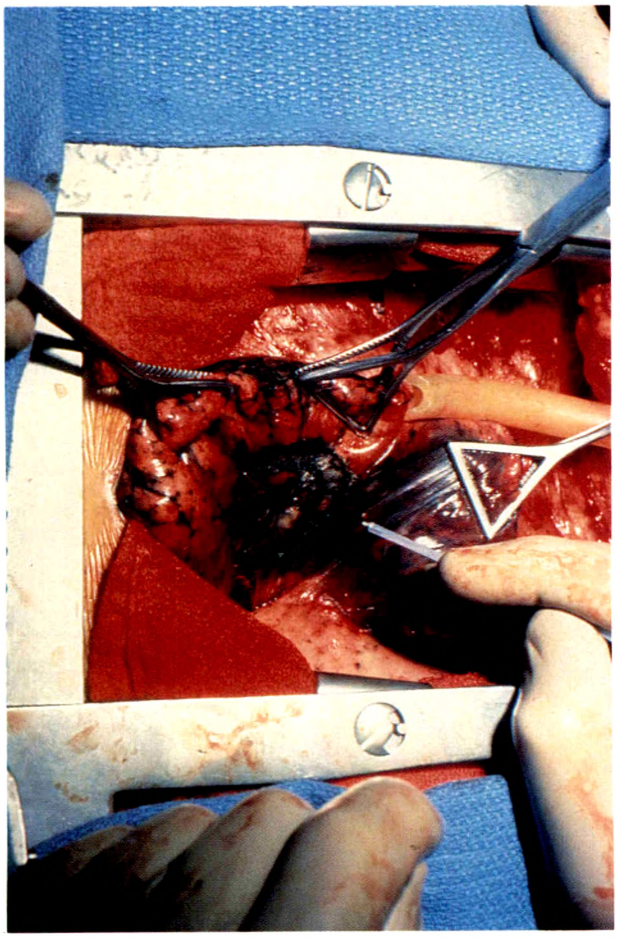

Fig 3. *Neodymium:yttrium-aluminum garnet laser incision circumscribing the pleural margin of a 3.5-cm pulmonary nodule near the inferior pulmonary ligament of the right lower lobe.*

monary blood supply or bronchial tree will potentially defunctionalize the pulmonary parenchyma about the resected mass. The Nd:YAG laser was employed to develop the line of resection and seal small pulmonary vessels and air spaces between segments for the 3 patients undergoing an anatomical segmental resection [11, 12]. The Nd:YAG laser can effectively seal most terminal bronchi and pulmonary vessels less than 3 mm in diameter; however, larger structures will require ligation with fine (4-0) suture to secure hemostasis and prevent major bronchopleural fistulas.

A smoke-filtration system ("Point One"; Stackhouse, Inc, Los Angeles, CA) was used to clear the operative field during the dissection. After complete removal of the lesion, the visceral pleural margins of the area of parenchymal resection were approximated in the first 4 patients. This step was subsequently deleted from other resections without increasing the occurrence of postoperative parenchymal air leaks. Two 28F chest tubes placed on 20 cm of underwater-seal suction drainage were inserted into the hemithorax before closure of the chest. Bilateral chest tube drainage was used in patients with a median sternotomy.

Results

The average operative time (165 ± 81.431 minutes [± standard deviation]) was not greatly prolonged with use of the Nd:YAG laser relative to standard pulmonary resections with mechanical stapling devices. The energy used averaged 31,977 J (± 25,390.5 J). Intraoperative blood loss was minimal (163.8 ± 111.194 mL). Postoperative air leaks were minimal (intermittent bubbling on or off suction) after most Nd:YAG laser resections, although 5 patients experienced moderate (bubbling present with every breath) early air leaks [3]. The mean duration of postoperative chest tube drainage (5.5 ± 4.1 days) and the mean postoperative hospital stay (10.5 ± 4.65185 days) were comparable with those after other pulmonary resections. The overall preoperative mean forced expiratory volume in 1 second among patients undergoing Nd:YAG laser resection alone of pulmonary lesions was 2.26 ± 0.5. There was no clinically significant difference between the mean postoperative forced expiratory volume in 1 second of 1.86 ± 0.52 and the preoperative values in these

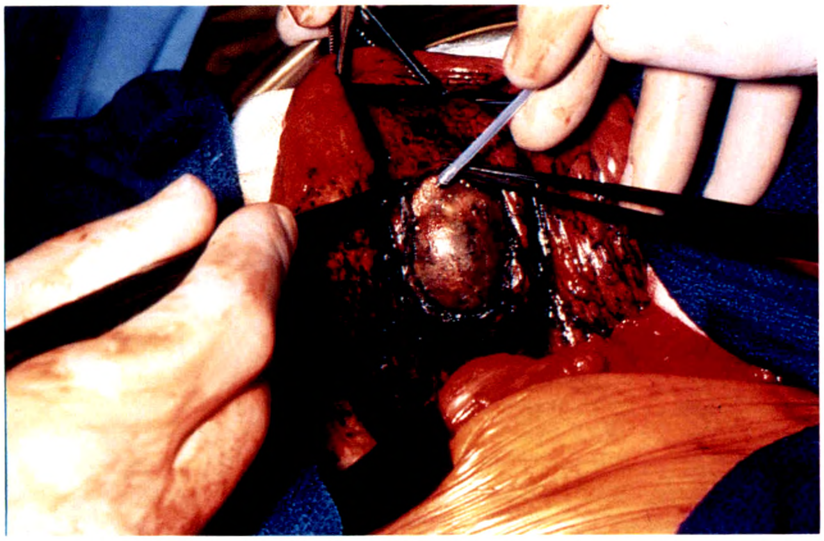

Fig 4. *Neodymium:yttrium-aluminum garnet laser beam being applied to the pulmonary parenchymal bed at the margin of resection to achieve a coagulative effect on small vessels and bronchioles.*

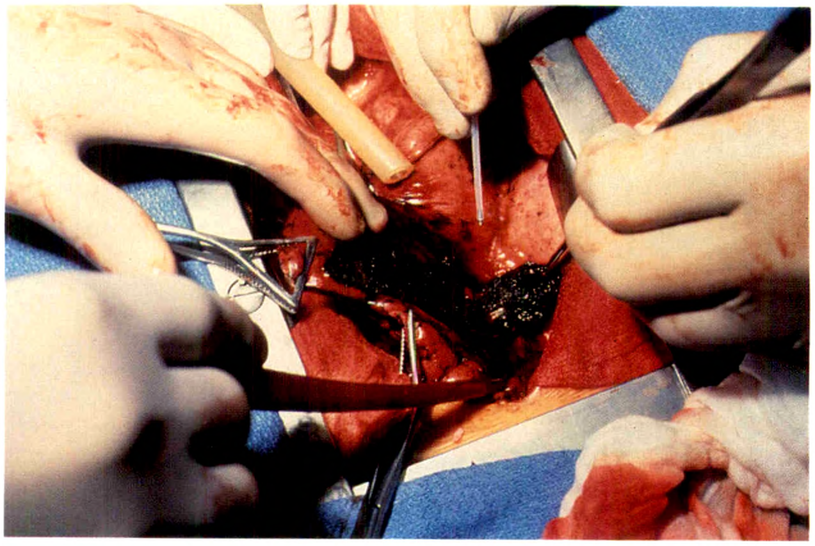

Fig 5. Deep pulmonary lesion being resected from the left lower lobe by neodymium:yttrium-aluminum garnet laser coagulation and evaporation of tissue at the margin of resection aided by gentle traction between lesion and surrounding normal pulmonary tissue.

patients. Although the numbers are small (n = 6) and the follow-up is short (longest follow-up, 11 months), there has been no evidence of local recurrence of malignant disease among these 9 patients undergoing Nd:YAG laser resection alone to manage pulmonary malignancies.

Postoperative complications were few. Lobar atelectasis requiring therapeutic bronchoscopy developed in 2 patients. In 1 patient who had right lower lobectomy for carcinoma, middle lobe torsion and gangrene developed and necessitated delayed lobectomy. Another patient required postoperative antiarrhythmic drug therapy to manage supraventricular tachycardia and atrial fibrillation. There were no deaths, major infections, or major postoperative bleeding among these patients treated with Nd:YAG laser–assisted pulmonary resection.

Comment

Limited pulmonary resection has been advocated by several authors [6, 12–14] as an effective means of managing patients with peripheral stage I carcinoma of the lung. Proper patient selection is critical to success with this surgical approach, and for the time being, lobectomy must still be considered the procedure of choice for most patients who are candidates for pulmonary resection [15, 16]. We emphasize that hilar and mediastinal lymph node sampling (or dissection) is a vital component of the management of these patients treated with limited Nd:YAG laser–assisted pulmonary resection. Certainly more than any other known variable, the presence of metastatic nodal involvement has the greatest prognostic significance for patients undergoing resection of pulmonary malignancies. Miller and Hatcher [17] demonstrated a 31% 5-year survival among patients with severe respiratory impairment managed with limited pulmonary resections. Jensik and colleagues [12, 13] reported a 5-year survival rate of 53% among patients with stage I lesions treated with segmentectomy. A similarly good outcome has been described for subgroups of patients with metastatic sarcomatous pulmonary lesions [18].

At this time, the Nd:YAG laser appears to be the most effective laser available for pulmonary resection. The carbon dioxide laser requires a bloodless field to be effective. The limited depth of pulmonary parenchymal penetration by this laser wavelength may also result in an insufficient coagulated seal to reliably prevent parenchymal air leaks [19]. The use of electrocautery excision of pulmonary nodules is a nonlaser option used by others [20] that is considerably more time-consuming and may also be less reliable in sealing parenchymal air leaks [19, 21]. The Nd:YAG laser causes deeper thermal effects (up to 4 mm), which may destroy microscopic local tumor extension and micrometastases in addition to sealing small vessels and air spaces [3].

The coagulated margin of pulmonary tissue after Nd:YAG lasing appears to heal as fast and as completely as areas undergoing carbon dioxide lasing or electrocautery resections [19, 22, 23]. This coagulating characteristic of the Nd:YAG laser makes it especially useful when operation is necessary to manage pulmonary bullous disease. The defocused Nd:YAG laser beam applied to the emphysematous tissue can cause thickening and leathery transformation of the more normal rim of pulmonary tissue around the bullous disease, and this can facilitate a more secure closure of ruptured blebs than can mechanical stapling techniques alone. Spraying the Nd:YAG laser beam over small to moderate-sized (less than 1 cm in diameter) pulmonary bullae can further result in collapse and obliteration of these pleura-based processes without air leak or the need of other surgical intervention. We have found this conditioning of the surrounding lung tissue to be a great improvement over the previous option of direct stapling or hand sewing of these friable, thin tissues.

The management of patients with limited pulmonary reserve and those with multiple metastatic lesions undergoing surgical resection can be particularly benefited by the pulmonary parenchyma–sparing properties of this laser technique. Possibly the greatest application for this technique is in the approach to undiagnosed deep-seated pulmonary nodules that heretofore required lobectomy for removal. Stapler resection of such lesions is prone to substantial distortion of and mechanical impingement on the remaining bronchopulmonary tissues [5, 24, 25]. We now limit our use of mechanical staplers to resection of small (less than 3 cm) peripheral lesions located on the edge of the lung and to completing poorly developed interlobar fissures during the course of pulmonary lobectomy.

In conclusion, we have found the Nd:YAG laser to be an effective tool for limited pulmonary resection and an important adjunct to the use of mechanical stapling and electrocautery excision of pulmonary nodules. This technique has been useful in extending the possibility of safe pulmonary resection among patients with marginal pulmonary reserve [3, 4]. Use of Nd:YAG laser resection for peripheral pulmonary lesions combined with limited thoracic incisions [26] and aggressive control of postoperative pain may allow safer yet equally effective surgical treatment of many patients with bronchogenic carcinoma of the lung.

We thank Julie Brown, RN, BSN, for data collection and Wendy Coffey for secretarial assistance.

References

1. Parr GVS, Unger M, Trout RG, Atkinson WG. One hundred neodymium–YAG laser ablations of obstructing tracheal neoplasms. Ann Thorac Surg 1984;38:374–81.
2. Gelb AF, Epstein JD. Neodymium–yttrium-aluminum-garnet laser in lung cancer. Ann Thorac Surg 1987;43:164–7.
3. LoCicero J III, Frederiksen JW, Hartz RS, Michaelis LL. Laser-assisted parenchyma sparing pulmonary resection. J Thorac Cardiovasc Surg 1989;97:732–6.
4. Moghissi K. Local excision of pulmonary nodular (coin) lesion with noncontact yttrium-aluminum-garnet laser. J Thorac Cardiovasc Surg 1989;97:147–51.
5. Roe BB. Discussion of Erret et al [6].
6. Erret LE, Wilson J, Chiu RC-J, Munro DD. Wedge resection as an alternative procedure for peripheral bronchogenic carcinoma in poor-risk patients. J Thorac Cardiovasc Surg 1985;90:656–61.
7. Fisher JC. The power density of a surgical laser beam: its meaning and measurement. Lasers Surg Med 1983;2:301–4.
8. Fuller TA. The characteristics in operation of surgical lasers. Surg Clin North Am 1984;64:843–9.
9. Kent EM, Blades B. The anatomic approach to pulmonary resection. Ann Surg 1942;116:257–68.
10. Overholt RH, Langer L. A new technique for pulmonary segmental resection. Its application in the treatment of bronchiectasis. Surg Gynecol Obstet 1947;84:257–68.
11. Kittle CF. Atypical resections of the lung: bronchoplasties, sleeve resections, and segmentectomies—their evolution and present status. Curr Probl Surg 1989;26:109–19.
12. Jensik RJ. The extent of resection for localized lung cancer: segmental resection. In: Kittle CF, ed. Current controversies in thoracic surgery. Philadelphia: W.B. Saunders, 1986: 171–5.
13. Jensik RJ, Faber LP, Kittle CF. Segmental resection for bronchogenic carcinoma. Ann Thorac Surg 1979;28:475–83.
14. Bennett WF, Abbey Smith R. Segmental resection for bronchogenic carcinoma: a surgical alternative for the compromised patient. Ann Thorac Surg 1979;27:169–72.
15. Martini N, Beattie EJ Jr. Results of surgical treatment in stage I lung cancer. J Thorac Cardiovasc Surg 1977;74:499–505.
16. Wilkins EW Jr, Scannell JG, Craver JG. Four decades of experience with resections for bronchogenic carcinoma at the Massachusetts General Hospital. J Thorac Cardiovasc Surg 1978;76:364–9.
17. Miller JI, Hatcher CR Jr. Limited resection of bronchogenic carcinoma in the patient with marked impairment of pulmonary function. Ann Thorac Surg 1987;44:340–3.
18. Mountain CF, McMurtrey MJ, Hermes KE. Surgery for pulmonary metastasis: a 20-year experience. Ann Thorac Surg 1984;38:323–30.
19. LoCicero J III, Hartz RS, Frederiksen JW, Michaelis LL. New applications of the laser in pulmonary surgery: hemostasis and sealing of air leaks. Ann Thorac Surg 1985;40:546–50.
20. Cooper JD, Perelman M, Todd TRJ, Ginsberg RJ, Patterson GA, Pearson FG. Precision cautery excision of pulmonary lesions. Ann Thorac Surg 1986;41:51–3.
21. Shields TW. Discussion of Cooper et al [20].
22. Minton JP, Andrews NC, Jesseph JE. Pulsed laser energy in the management of multiple pulmonary metastases. J Thorac Cardiovasc Surg 1967;54:707–12.
23. Wolfe WG, Cole PH, Sabiston DC. Experimental and clinical use of the YAG laser in the management of pulmonary neoplasms. Ann Surg 1984;199:526–31.
24. Shields TW. Discussion of Erret et al [6].
25. Hood RM. Stapling techniques involving lung parenchyma. Surg Clin North Am 1984;64:469–80.
26. Hazelrigg SR, Landreneau RJ, Boley TM, et al. The effects of muscle sparing versus standard posterolateral thoracotomy on pulmonary function, muscle strength, and postoperative pain. J Thorac Cardiovasc Surg 1991;101:394–401.

INVITED COMMENTARY

Less-than-lobectomy resection of stage I primary pulmonary carcinoma is now an established procedure for use in patients with compromised lung function. Excision of single or multiple metastatic pulmonary nodules has also been shown to be effective if the primary lesion is controlled. Finally, minimal pulmonary resection of unknown lesions is appropriate to establish a diagnosis and for definitive therapy in the case of benign lesions. The issue at hand is how best to accomplish the goals of complete eradication safely and expeditiously with minimal morbidity and mortality.

Anatomical segmental resection has been an effective method of achieving these goals. Pulmonary tuberculosis was the disease admirably suited for this method. However, the decline of tuberculosis has resulted in few of these resections now being performed, and many thoracic surgeons are not familiar with this method.

Wedge excision using vascular clamps has been employed as a substitute for segmental resection and has also been used for those lesions that were not amenable to anatomical resection. Reinforcement of suture lines with Teflon felt bolsters has added to the efficacy of this technique.

The availability of stapling devices led to their use in partial pulmonary resections. Precise electrocautery division of pulmonary parenchyma either along segmental planes or otherwise is also an effective method.

With the advent of lasers it was natural to expect that they would be used for pulmonary resection. They have; witness the report of Landreneau and associates.

Even lasers are now "older technology." A recent presentation at the meeting of The Society of Thoracic Surgeons documented the experience of one group using a Cavitron Ultrasonic Suctioning Aspirator for lung resection.

Of interest is that authors describing each technique purport their method to be superior to others in terms of sparing parenchyma, fewer air leaks, less blood loss, and short postoperative thoracostomy tube drainage. Is one method superior to another and deserving of exclusive use in the problem areas described? Probably not. I have had the opportunity to use all of these methods, except the Cavitron Ultrasonic Suctioning Aspirator, and it is my opinion that a well-trained thoracic surgeon should have knowledge of various methods and use them as appropriate to achieve his or her objectives. All these modalities are not available in all operating rooms. Some are expensive, particularly lasers and the Cavitron Ultrasonic Suctioning Aspirator. Even staples are expensive. Each surgeon has to determine whether the cost of the method justifies the supposed benefits.

Landreneau and associates have documented their experience with the use of a Nd:YAG laser applied to a variety of pathological conditions with good results. Whether this method is superior to other techniques is unclear. The role of the Nd:YAG laser in pulmonary resectional surgery is yet to be established conclusively. On the basis of this report, surgeons should not feel compelled to purchase a laser for use in these circumstances. Instead, those of us who have access to lasers should continue to investigate this modality to determine the necessity and appropriateness of its use.

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Current Surgical Technique to Repair Fallot's Tetralogy With Absent Pulmonary Valve Syndrome

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The experience with surgical repair of Fallot's tetralogy and absent pulmonary valve syndrome is reviewed. Twenty-two patients aged 1 day to 8 years were treated between 1982 and 1989 using one surgical technique. This consisted of resection of the main pulmonary artery and large parts of the anterior wall of the right and left pulmonary artery. The ventricular septal defect was closed with a patch, and an aortic or pulmonary homograft (size, 8 to 24 mm) was interposed between the right ventricle and the pulmonary artery. Two of the 8 infants operated on died; there was one late death. All 14 older children survived the operation. All survivors are well up to 7 years follow-up (mean follow-up, 3.6 years). We recommend early treatment of infants; older children can be treated electively. The technique used in our series gives excellent results.

(Ann Thorac Surg 1991;51:979–82)

Absent pulmonary valve syndrome (APVS) is a rare variant of Fallot's tetralogy. It is characterized by a ventricular septal defect that is usually located in the outlet septum; the pulmonary valve is either absent or rudimentary but there is usually a degree of obstruction at the pulmonary valve ring level or within the outflow tract of the right ventricle. Pulmonary arteries are grossly dilated with exaggerated pulsations; this often causes severe obstruction of one or both main bronchi.

Patients are seen in two well-defined groups: infants with severe respiratory symptoms often are seen in the neonatal period. Morbidity and mortality in this group is high [1–6]. The second group is composed of older children whose symptoms are less severe. Elective operations can usually be delayed.

Medical treatment of sick infants is usually unsuccessful [7, 8]. In the past various surgical techniques were suggested and tried. They included palliative [9–14] and corrective [2, 15–19] procedures. We have favored total repair of patients with APVS, irrespective of age and symptoms, and have published our results using several surgical techniques in 1986 [16].

The purpose of this communication is to review our results since January 1982 using a standardized approach.

Material and Methods

Patients

Twenty-two patients with APVS were operated on between January 1982 and December 1989. Eight were infants younger than 1 year (aged 1 day to 11 months). Fourteen were children older than 1 year (age range, 2 to 8 years). Two infants and 2 older children were included in our previous communication [16].

All patients in the infant group had severe respiratory symptoms and congestive heart failure. Several infants did not respond to medical therapy and were admitted on an emergency or semiemergency basis for urgent treatment. Older children had mild respiratory or cardiac symptoms or both. They were managed medically, and operation was performed electively at an older age.

Clinical findings included a pansystolic murmur and low-pitched diastolic murmur at the left sternal border. Second pulmonary sound was absent. Chest roentgenography showed cardiomegaly and gross dilatation of the main, left, and right pulmonary arteries in all. Pulmonary vascularity was normal or slightly reduced. Four of 8 infants had severe air trapping on chest roentgenography (Table 1). Two of them had to be mechanically ventilated before operation; 1 underwent lobectomy in another hospital before admission to our department. All infants and children underwent two-dimensional echocardiography and Doppler assessment. In addition, cardiac catheterization and angiography was performed on all but 1 sick neonate. This, in retrospect, proved to be an error. This patient had grossly hypoplastic peripheral pulmonary arteries with branching anomalies and clearly inoperable disease. He died on the operating table. Abnormalities of his pulmonary vascular tree were elucidated by postmortem angiocardiography (Fig 1).

Angiography confirmed the diagnosis by demonstrating the ventricular septal defect and gross dilatation of the pulmonary arteries. Peak systolic right ventricular to pulmonary arterial pressure gradient varied from 32 to 85 mm Hg (mean, 56 mm Hg) in the group of infants and 50 to 110 mm Hg (mean, 72 mm Hg) in the group of older children. Associated cardiac anomalies included absence

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Table 1. Data on 8 Infant Patients

Patient No.	Age	Symptoms	Chest Roentgenogram	Angiogram	Outcome	Extubated
1	5 mo	Severe respiratory failure; recurrent chest infection	Hyperinflated right middle lobe	Large MPA	Right middle lobectomy 4 days after operation; well	14 d
2	3 mo	Severe respiratory failure; cyanosis	Hyperinflated right lower lobe	Aneurysmal dilated PAs	Well	3 d
3	27 d	Ventilated since birth	Hyperinflated right upper and middle lobe	Large right PA with abnormal branching	Right upper and middle lobectomy 7 days after operation; died at 3 mo	. . .
4	9 mo	Heart failure, respiratory failure	Enlarged heart, enlarged central PAs	Large PAs	Well	2 d
5	11 mo	Recurrent chest infection, cyanosis	Enlarged central PAs	Grossly dilated PAs	Died at 14 d	. . .
6	6 mo	Severe respiratory failure	Hyperinflation both lungs	Huge main PA	Well	4 d
7	1 d	Cyanosis, low cardiac output, acidosis; ventilated	Enlarged heart, large central PAs	. . .	Died on table	. . .
8	7 mo	Severe respiratory, cyanosis; lobectomy elsewhere age 6 mo	Large PA	Large PAs	Well	2 d

PA = pulmonary artery.

of left pulmonary artery in 1, major aortopulmonary collaterals in 1, and DiGeorge syndrome in 2 patients.

Surgical Technique

The main pulmonary artery was resected and the anterior wall of the right and left pulmonary artery was resected to reduce their size. Resection was carried out to the hilum of both lungs, close to the origin of upper lobe arteries (Fig 2). Suturing the edges of the resected right and left pulmonary arteries considerably reduced their size. Plication of the posterior wall of the right and left pulmonary artery was not performed in any of our patients. Incision was then extended into the right ventricular outflow tract. Ventricular septal defect was closed with a polytetrafluoroethylene (Gore-Tex) patch and running 4.0 or 5.0 polypropylene suture.

Aortic or pulmonary homograft was interposed between the right ventricle and the bifurcation of the pulmonary artery. Right ventricular outflow tract was reconstructed either with the anterior cusp of the mitral valve of the homograft or with a pericardial patch. The size of the homograft varied between 8 and 24 mm.

Results

Infants

Two of 8 infants operated on died. One was a 1-day-old neonate who was operated on without cardiac catheterization and angiocardiography. Right and left pulmonary arteries were grossly dilated. Dilatation ended abruptly in the hilum, and intrapulmonary branches of both right and left pulmonary arteries were severely hypoplastic. The patient could not be weaned off cardiopulmonary bypass. Postmortem angiography showed severe hypoplasia of peripheral pulmonary arteries on both sides with gross abnormalities in pulmonary branching pattern (see Fig 1). There was no blood supply to the right lower lobe, and branching into the right upper lobe and the left lung was abnormal.

The second death occurred in a 3-week-old infant who suffered renal failure after operation. He died 2 weeks later in multiorgan failure. In addition, there was one late death. A premature infant, aged 1 month and weighing 1.8 kg, was treated in another hospital abroad. After 1 month of intermittent positive-pressure ventilation he

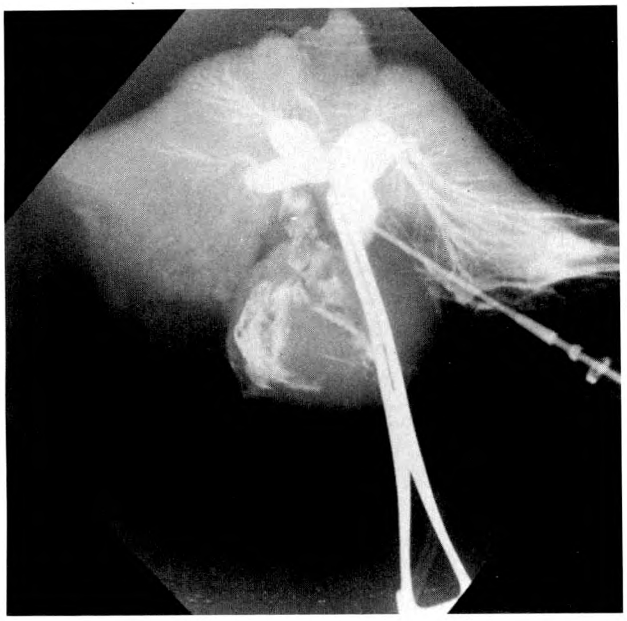

Fig 1. Postmortem pulmonary angiogram shows grossly dilated main, right, and left pulmonary arteries. There is no blood supply to the right lower lobe, and intraparenchymal branches to the rest of the lung are abnormal, narrow, and "spidery."

was transferred to us for surgical treatment. On admission, there was severe air trapping in the right upper and middle lobes. The patient underwent uneventful repair: the ventricular septal defect was closed with a Gore-Tex patch, and an 8-mm pulmonary homograft was interposed between the right ventricle and the pulmonary artery after reduction of the size of both right and left pulmonary arteries. Seven days after the operation, the air trapping caused severe respiratory embarrassment and emergency right upper and middle lobectomy had to be performed. After this operation the child's condition gradually improved and he was weaned off the ventilator to continuous positive airway pressure. He was then transferred back to the referring hospital. Unfortunately, extubation was not possible. The child gradually required increased ventilation, and 2 months after operation the child was restudied. Aneurysm of the homograft was found with severe reduction of the peripheral pulmonary artery sizes. The patient underwent reoperation, and the homograft was exchanged for a new one (12 mm). Unfortunately, the suprasystemic pressure in the right ventricle was reduced to the systemic level and the patient died 2 days later, presumably because of gross abnormalities in the size and branching pattern of intraparenchymal pulmonary arteries.

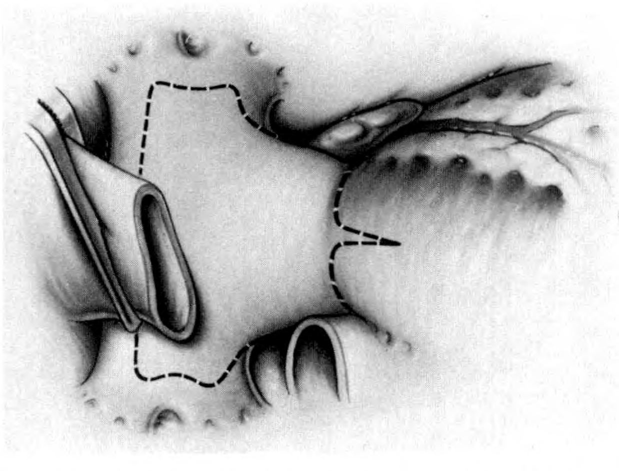

Fig 2. Important features of surgical technique, namely, the resection of the main pulmonary artery and the anterior wall of the right and left pulmonary artery (indicated by dotted line*), are illustrated. The ascending aorta is shown as transected; this is for the purpose of illustration only—to show the full extent of the pulmonary artery excision.*

Children

All 14 children survived the operation. Their postoperative course was generally uneventful, and they were extubated after 1 to 3 days (mean, 1.2 days).

Late Results

Follow-up up to 7 years (mean, 3.6 years) was available in all survivors. All patients operated on after the age of 1 year were symptom-free. No reoperations have been required so far. One of the 5 surviving infants has severe developmental retardation. This patient was recatheterized in December 1988. The conduit was unobstructed, and the right ventricular to left ventricular ratio was 0.5. His symptoms were obviously related to the developmental retardation rather than to any residual or recurrent hemodynamic lesion.

Comment

Absent pulmonary valve syndrome can be diagnosed accurately with two-dimensional echocardiography. We use echocardiography without additional invasive investigation for an increasing number of children with various congenital heart defects [20]. There are, however, certain limitations to this technique, and evaluation of peripheral and intraparenchymal pulmonary arteries is one of them. The 1 infant in our series who did not undergo preoperative angiography (Fig 1) is a good example. This confirms our belief that angiography is a useful, and in some cases essential, investigation of infants with APVS.

Abnormalities of hilar branches of the pulmonary artery in APVS were demonstrated on postmortem pulmonary angiography by Rabinovitch and associates [21]. They found that instead of single segmental arteries there were tufts of arteries that entwined and compressed interpulmonary bronchi. Rabinovitch and associates also found impaired alveolar multiplication. On the basis of their data they [21] suggest that these abnormalities of interparenchymal pulmonary arteries may be responsible for continuing symptoms in some infants even after relief of compression of the main bronchi.

The difference in the severity of symptoms between infants and older children with APVS was observed by several authors [2, 4, 6, 22]. High mortality rates in infants with APVS led several surgeons to try various palliative or two-stage procedures [1, 8, 9, 13]. Byrne and co-workers [10] successfully treated a 6-week-old infant by ligation of the pulmonary artery and creation of a central shunt. The same basic approach using a modified Blalock-Taussig shunt was used by Ilbawi and associates [11] in 4 infants; 2 survived. Opie and colleagues [14] and Park and Trinkle [12] banded the pulmonary artery successfully in 3 infants with APVS.

The authors recommending total repair of this anomaly agree that the ventricular septal defect should be closed and right ventricular outflow tract obstruction relieved. There is, however, no general consensus whether a pulmonary valve should be inserted and the size of the pulmonary arteries should be reduced. McCaughan and co-workers [2] recommended insertion of a pulmonary valve and plication of aneurysmal pulmonary arteries in infants with APVS. In older children they believe both these steps are not necessary. Ilbawi and associates [4, 11] recommended pulmonary valve insertion in the older group. For infants they prefer palliation first. Insertion of a pulmonary valve was also recommended by Layton and co-workers [15] and Mavroudis and colleagues [18], whereas Stellin and associates [17] place more emphasis on reduction of pulmonary artery size by anterior resection and posterior plication.

In our previous experience we have treated patients with APVS by closing the ventricular septal defect, but the approach to the pulmonary valve varied. We have placed some outflow tract patches, heterograft valves, and aortic or pulmonary homografts. In general, pulmonary arterial size was not reduced. Since 1982 we have used a fairly uniform technique consisting of ventricular septal defect closure, placement of a homograft, and reduction of the size of the pulmonary arteries, although we have not used posterior wall plication as suggested by Stellin and associates [17].

We continue using this technique. The problems are encountered in the group of youngest infants who may have gross anatomical anomalies in the size and distribution of the pulmonary arteries. In some of them early bronchomalacia develops, and this may necessitate lobectomy in addition to the intracardiac repairs. Although we are pleased with the overall results (19 long-term survivors among 22 patients operated on), we cannot draw definite conclusions about the group of young infants as the numbers are too small.

References

1. Waldhausen JA, Friedman S, Nicodemus H, Miller WW, Rashkind W, Johnson J. Absence of the pulmonary valve in patients with tetralogy of Fallot. Surgical management. J Thorac Cardiovasc Surg 1969;57:669–74.
2. McCaughan BC, Danielson GK, Driscoll DJ, McGoon DC. Tetralogy of Fallot with absent pulmonary valve. Early and late results of surgical treatment. J Thorac Cardiovasc Surg 1985;89:280–7.
3. Fischer DR, Neches WH, Beerman LB, et al. Tetralogy of Fallot with absent pulmonic valve. Analysis of 17 patients. Ann J Cardiol 1984;53:1433–7.
4. Ilbawi MN, Idriss FS, Muster AJ, Wessel HU, Paul MH, DeLeon SY. Tetralogy of Fallot with absent pulmonary valve. J Thorac Cardiovasc Surg 1981;81:906–15.
5. Emmanoulides GC, Thanopoulos B, Siassi B, Fishbein M. "Agenesis" of ductus arteriosus associated with the syndrome of tetralogy of Fallot and absent pulmonary valve. Am J Cardiol 1976;37:403–9.
6. Pinsky WW, Nihill MR, Mullins CE, Harrison G, McNamara DG. The absent pulmonary valve syndrome. Circulation 1978;57:159–62.
7. D'Cruz IA, Arcilla RA, Agustsson MH. Dilatation of the pulmonary trunk in stenosis of the pulmonary valve and of the pulmonary arteries in children. Am Heart J 1964;68:612.
8. Osman MZ, Merg CCL, Girdany BR. Congenital absence of the pulmonary valve. Report of eight cases with review of the literature. AJR 1969;106:58–69.
9. Litwin SB, Rosenthal A, Fellows K. Surgical management of young infants with tetralogy of Fallot, absence of the pulmonary valve and respiratory distress. J Thorac Cardiovasc Surg 1973;65:552–8.
10. Byrne JP, Hawkins JA, Battiste CE, Khoury GH. Palliative procedures in tetralogy of Fallot with absent pulmonary valve. A new approach. Ann Thorac Surg 1982;33:499–502.
11. Ilbawi MN, Fedorchik J, Muster AJ, et al. Surgical approach to severely symptomatic newborn infants with tetralogy of Fallot and absent pulmonary valve. J Thorac Cardiovasc Surg 1986;91:584–9.
12. Park MK, Trinkle JK. Absent pulmonary valve syndrome: a two stage operation. Ann Thorac Surg 1986;41:669–71.
13. Bove EL, Shaher RM, Alley R, McKneally M. Tetralogy of Fallot with absent pulmonary valve and aneurysm of the pulmonary artery: report of two cases presenting as obstructive lung disease. J Pediatr 1972;81:339–43.
14. Opie JC, Sandor GG, Ashmore PG, Patterson MW. Successful palliation by pulmonary artery banding in absent pulmonary valve syndrome with aneurysmal pulmonary arteries. J Thorac Cardiovasc Surg 1983;85:125–8.
15. Layton A, McDonald A, McDonald L, Towers M, Weaver D, Yacoub M. The syndrome of absent pulmonary valve. Total correction with aortic vascular homografts. J Thorac Cardiovasc Surg 1972;63:800–8.
16. Karl TR, Musumeci F, de Leval M, Pincott JR, Taylor JFN, Stark J. Surgical treatment of absent pulmonary valve syndrome. J Thorac Cardiovasc Surg 1986;91:590–7.
17. Stellin G, Jonas RA, Goh TH, Brawn WJ, Venables AW, Mee RB. Surgical treatment of absent pulmonary valve syndrome in infants: relief of bronchial obstruction. Ann Thorac Surg 1983;36:468–75.
18. Mavroudis C, Turley K, Stanger P, Ebert PA. Surgical management of tetralogy of Fallot with absent pulmonary valve. J Cardiovasc Surg 1983;24:603–9.
19. Arensman FW, Francis PD, Helmsworth JA, Benzing G. Early medical and surgical intervention for tetralogy of Fallot with absence of pulmonic valve. J Thorac Cardiovasc Surg 1982;84:430–6.
20. Stark J, Smallhorn J, Huhta J, de Leval M. Surgery for congenital heart defects diagnosed with cross-sectional echocardiography. Circulation 1983;68(Suppl 2):129–38.
21. Rabinovitch M, Grady S, David I, et al. Compression of intrapulmonary bronchi by abnormally branching pulmonary arteries associated with absent pulmonary valves. Am J Cardiol 1982;50:804–13.
22. Lakier JB, Stranter P, Heymann MA, Hoffman JI, Rudolph AM. Tetralogy of Fallot with absent pulmonary valve. Natural history and haemodynamic considerations. Circulation 1974;50:167–75.

Morbidity and Mortality After Coronary Artery Bypass in Octogenarians

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One hundred fifty seven consecutive octogenarians (mean age ± standard deviation, 82.4 ± 1.9 years) underwent coronary artery bypass grafting with hypothermia (mean temperature, 21.8° ± 1.8°C), hyperkalemic cardioplegia, and cardiopulmonary bypass in a 9-year period. Sixty-six percent were male. Preoperatively, 115 patients (73%) were in New York Heart Association functional class IV, with the remainder being in either class III (23%) or class II (4%). Twenty percent of the patients had major complications including postoperative hemorrhage (15), sepsis (9), cerebrovascular accident (6), third-degree heart block (5), renal failure requiring dialysis (1), and pulmonary embolism (1). The 30-day or in-hospital mortality rate was 7.0%. Mean total hospital stay was 26.1 ± 17.9 days. One-year and 5-year actuarial survival rates were 85% and 62%, respectively. Higher mortality was seen to be associated with New York Heart Association class IV, left ventricular ejection fraction less than 0.40, and lesser values for cardiac output and cardiac index. At the 6-month postoperative follow-up, 73% of the survivors reported that their general health had improved as compared with before operation. This experience demonstrates that for select octogenarians with unmanageable angina pectoris, coronary artery bypass grafting is an effective therapeutic option.

(Ann Thorac Surg 1991;51:983–6)

Elderly patients (older than 65 years) constituted 11% of our population in 1981, with a trend to increase yearly [1]. According to the 1980 census, 43% of all Americans will reach the age of 80 years and live for an average of 8 more years [2]. Approximately 40% of all octogenarians have symptomatic cardiovascular disease, including 18% with ischemic heart disease [3, 4]. Many of these elderly patients still enjoy productive lives, limited only by their symptomatic coronary artery disease. Recent reports indicate that coronary artery bypass grafting for select elderly individuals who otherwise are in good physical and mental health has substantially decreased mortality and morbidity, and improved quality of life [5–21]. To more precisely define the preoperative characteristics and postoperative experiences of octogenarians undergoing isolated coronary artery bypass grafting, we have reviewed our recent experience.

Material and Methods

In the 9-year period from October 1980 to September 1989, 157 consecutive patients 80 years of age or older underwent isolated coronary artery bypass grafting using cardiopulmonary bypass.

Data on patient characteristics, coronary risk factors, surgical procedures, complications, and mortality were routinely collected for all patients. Patients were then followed up by mailed questionnaires sent 6 months after operation and annually thereafter. The follow-up evaluations included assessment of survival status, an evaluation of general health as compared with before operation (improved, the same, worse), and an assessment of current level of activity (very active, moderately active, sedentary, or restricted). For patients who had died, cause of death was recorded as ascertained by their referral physicians.

Acute deaths were defined as in-hospital deaths or deaths within 30 days of operation. Statistical tests were carried out to compare survivors with nonsurvivors with respect to patient and operative characteristics. Tests include two-sample *t* tests for continuous factors such as cardiac output, and Fisher's exact test or the likelihood ratio χ^2 test for categorical factors. In all statistical tests, a p value of 0.05 or less was considered significant. Life-table survival analysis was used to estimate survival rates at 1 year and 5 years postoperatively. Cox adjusted survival analyses were used to identify patient and operative characteristics that were predictive of survival. These analyses used the BMDP statistical programs P1L and P2L [22]. Factors included in the Cox analysis were age, sex, New York Heart Association (NYHA) functional class (class I to III versus IV), cardiac index and output, method of cardioplegia, use of an internal mammary artery graft, if the ejection fraction was less than 0.40, if intraaortic balloon counterpulsation was used, ischemic

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time, total cardiopulmonary pump time, and minimum temperature during operation.

Results

Patient and Operative Characteristics

Octogenarian patients represented 5% of all coronary artery bypass operations done during the study period. There was an increasing trend over this period going from 1% in 1981 to 8% in 1989.

Of the 157 patients studied, 66% were male; the mean age was 82.4 ± 1.9 years (standard deviation), with the oldest patient being 88 years old. Preoperatively, most of the patients (73%) were in NYHA functional class IV; 23% were in class III and 4% were in class II. Of the 70 patients on whom preoperative ejection fractions were evaluated, 13% had ejection fractions of less than 0.40. Commonly reported preoperative risk factors include previous myocardial infarction (67%, 105 patients), hypertension (62%, 97), and diabetes mellitus (27%, 43). Although 51 patients (33%) smoked in the past, less than 5% were current smokers. The most common preoperative major symptoms were unstable progressive angina (84%), dyspnea (48%), chronic stable angina (35%), and abnormal exercise test (33%). Most patients were undergoing bypass grafting because of medically refractory symptomatic cardiac status. Four patients had a history of previous balloon angioplasty and 5 patients had a history of bypass grafting. Patients stayed in the hospital for a mean of 26.1 ± 17.9 days, with a maximum stay of 134 days; the mean operative stay was 19.1 ± 15.8 days.

Operative management included the use of systemic hypothermia, ranging from 17° to 28°C (mean temperature, 21.8° ± 1.8°C), and hyperkalemic crystalloid (115 patients) or hyperkalemic blood (32 patients) cardioplegia at approximately 4°C. All patients received saphenous vein or arm vein grafts; 32 patients (20%) also received one or two internal mammary artery grafts. The average number of grafts per patient was 3.4 ± 0.8, ranging from 1 to 6 grafts.

Complications

Surgical complications are summarized in Table 1. Twenty percent of the patients had major complications including postoperative hemorrhage (reoperation for bleeding, hemorrhage-related death, blood loss ≥ 250 mL/h) (9.6%), sepsis (5.7%), cerebrovascular accident (3.8%), third-degree heart block requiring pacemaker implantation (3.2%), renal failure requiring dialysis (0.6%), and pulmonary embolism (0.6%). Other complications included postoperative mental aberrations (14.6%), pericarditis (7.0%), and wound complications (15.3%). Ten patients (6.4%) were on intraaortic balloon counterpulsation.

Mortality

The 30-day or in-hospital mortality rate was 7.0% ± 2.0% (standard error). Ten of the 11 early deaths were in patients in NYHA functional class IV; 1 patient was in class III. Survival probabilities at 1 year and 5 years postoperatively were estimated as 85% ± 3% and 62% ± 5%, respectively, based on a life-table analysis. A review of all deaths ($n = 47$, mean follow-up of 32 months) indicated that 27 of 45 (60%) were cardiac related (Table 2). This does not include two deaths of unknown cause.

Factors identified as being predictive of 30-day or in-hospital death (Table 3) were lower cardiac output ($p < 0.001$) and lower cardiac index ($p < 0.001$). Factors predictive of increased overall survival using the Cox adjusted survival analysis were having a higher cardiac index ($p = 0.004$) and cardiac output ($p = 0.04$), not being in NYHA functional class IV ($p = 0.03$), and having a left ventricular ejection fraction greater than 0.40 ($p = 0.05$). Although the relationships between early death and both NYHA class and ejection fraction were not statistically significant, nonsurvivors had a greater proportion of patients in NYHA class IV (91% versus 72% in survivors) and ejection fraction of less than 0.40 (20% versus 12% in survivors). Use of intraaortic balloon counterpulsation

Table 1. Postoperative Complications ($n = 157$)

Complication	No. of Patients	Percent
Supraventricular arrhythmia		
Atrial fibrillation	68	43.3
Atrial flutter	29	18.5
Heart block		
RBBB	17	10.8
LBBB	8	5.1
Left anterior hemiblock	22	14.0
Second-degree block	3	1.9
Third-degree block[a]	5	3.2
Ventricular arrhythmia		
VT or VF	19	12.1
PVC requiring medication	18	11.5
Postoperative MI[b]	17	10.8
Pulmonary insufficiency	10	6.4
Transient renal insufficiency[c]	17	10.8
Wound complications	24	15.3
Postoperative hemorrhage[a]	15	9.6
Postoperative psychosis	23	14.6
Pericarditis	11	7.0
Pericardial tamponade	3	1.9
Sepsis[a]	9	5.7
Stroke (CVA)[a]	6	3.8
Sternal dehiscence	2	1.3
Renal failure requiring dialysis[a]	1	0.6
Peripheral vascular thrombosis	1	0.6
Pulmonary embolism[a]	1	0.6
Total major complications	31	19.8

[a] Major complication. [b] Myocardial infarction was diagnosed on the basis of new Q waves. [c] Defined as serum creatinine level ≥177 μmol/L (2 mg/dL).

CVA = cerebrovascular accident; LBBB = left bundle-branch block; MI = myocardial infarction; PVC = premature ventricular contraction; RBBB = right bundle-branch block; VF = ventricular fibrillation; VT = ventricular tachycardia.

was not significantly related to either early or total mortality, though 20% of the group with intraaortic balloon counterpulsation (2/10) versus 6% in the group without it (9/147) had died.

Causes of death are listed in Table 2. Pump failure, arrhythmias, either known or presumed, and cerebrovascular accidents accounted for five of 11 early deaths. Arrhythmia, heart failure, myocardial infarction, and pneumonia were responsible for 23 of 36 late deaths.

Quality of Life in Survivors

Of 112 patients who completed the 6-month follow-up questionnaire (mean follow-up, 7.5 months), 73% indicated that their general health had improved as compared with before operation; 13% reported being the same, and 14% reported being worse. With respect to current level of activity, 40% reported being very or moderately active, 26% sedentary, and 34% restricted. Sixty-eight percent reported that they exercise, and 78% reported that they either experience no shortness of breath (59%) or experience it only after moderate to strenuous exercise.

Comment

The 30-day or in-hospital death rate was 7.0%. One-year and 5-year actuarial survival rates were 85% and 62%, respectively. When all deaths were reviewed, 60% of the deaths were found to be cardiac related. This experience is not different from the 1.6% to 14% operative mortality that has been reported by other institutions for patients in the 70-year-and-over age category [5–21]. Our experience again supports the contention that for select octogenarians with unmanageable angina pectoris, coronary artery bypass grafting may be an alternative, although such patients do have a higher complication rate associated as much with their advanced NYHA class as with their age. Most octogenarians may tolerate coronary artery bypass grafting as well as younger individuals [13]. There is no reason why the approach to older patients with coronary arteriosclerotic heart disease should be any different than in younger patients at a comparable stage in their disease process. Problems such as increased mortality and complications occur when patients are allowed to advance to class IV status before operation is undertaken as a desperate measure.

Table 2. Causes of Death

Cause	Early	Late	Total
Cardiac related			
Myocardial infarction	0	4	4
Chronic heart failure	0	6	6
Arrhythmia or presumed	2	9	11
Pump failure with CHF	1	1	2
Cerebrovascular accident	2	2	4
Noncardiac related			
Pulmonary embolism	1	0	1
Pulmonary insufficiency or respiratory failure	1	0	1
Hemorrhage	2	0	2
Pneumonia	0	4	4
Suicide	0	1	1
Cancer	0	3	3
Hepatitis	0	2	2
Other noncardiac	1	1	2
Renal failure	0	1	1
Sepsis	1	0	1
Unknown	0	2	2
Total	11	36	47

CHF = congestive heart failure.

Table 3. Thirty-Day or In-Hospital Death Comparison of Survivors and Nonsurvivors

Factor	Alive (n = 146)	Dead (n = 11)	*p* Value
Age (mean ± SD)	82.4 ± 1.9	81.8 ± 1.6	0.26
Sex (% male)	66.4	63.6	1.00
NYHA class (%)			
I–III	28.1	9.1	0.29
IV	71.9	90.9	
IMA graft (%)	20.6	18.2	1.00
Ischemic time (min) (mean ± SD)	87 ± 26	79 ± 18	0.26
Pump time (min) (mean ± SD)	128 ± 37	123 ± 30	0.65
Hypothermia (mean ± SD)	21.7 ± 1.8	22.5 ± 1.4	0.14
Cardioplegia (%)			
Blood	21.7	22.2	1.00
St. Thomas	78.3	77.8	
Ejection fraction <0.40[a] (%)	12.3	20.0	0.51
Cardiac output (mean ± SD)[b]	4.33 ± 1.13	2.92 ± 1.23	<0.001
Cardiac index (mean ± SD)[b]	2.52 ± 0.64	1.68 ± 0.59	<0.001
IABP (%)	5.5	18.2	0.15

[a] Ejection fraction is available for 65 survivors and 5 nonsurvivors.
[b] Cardiac output and index values are available for 124 survivors and 9 nonsurvivors

IABP = intraaortic balloon pumping; IMA = internal mammary artery; NYHA = New York Heart Association; SD = standard deviation.

Morbid complications after coronary artery bypass grafting in aged patients are extremely important [23, 24]. There was a substantial percentage (20%, 30 patients) in whom major complications developed during the early (30-day) postoperative period. In our institution, routine monitoring of pulmonary artery pressure and cardiac output by means of the Swan-Ganz catheter has been added to the armamentarium to prevent postoperative fluid overload and maintain adequate preload, thereby minimizing the potential for postoperative hemodynamic, pulmonary, and renal complications.

Higher early mortality of coronary artery bypass grafting in the octogenarians was related to lower cardiac output ($p < 0.001$) and lower cardiac index ($p < 0.001$). Higher overall mortality was similarly related to these factors, in addition to NYHA functional class IV status ($p = 0.03$) and an ejection fraction less than 0.40 ($p = 0.05$).

In conclusion, elderly patients can be treated successfully with coronary artery bypass grafting as demonstrated by a 5-year actuarial survival rate of 62%. On this basis we believe that patient selection should be based on life expectancy in the individual patient in terms of other disease factors. Advanced cardiac status that accrues by delay of more aggressive surgical therapy in deference to advanced age is a particularly ominous factor. All other factors being equal, indication for and timing of coronary bypass grafting in octogenarians should be as for younger patients.

References

1. US Bureau of Census, Current Population Reports, Series p-25, No. 952. Projections of the population of the United States by age, sex, and race: 1983–2080. Washington, DC: Government Printing Office, 1984.
2. National Center for Health Statistics. United States life tables: US decennial life tables for 1979–1981, Vol 1, No 1. Washington, DC: Government Printing Office, 1985 (DHHS publication No. (PHS) 85-1150-1).
3. National health interview survey 1983–1985. Hyattsville, MD: National Center for Health Statistics, 1986.
4. National nursing home survey. Hyattsville, MD: National Center for Health Statistics, 1985.
5. Tsai TP, Matloff JM, Gray RJ, et al. Cardiac surgery in the octogenarian. J Thorac Cardiovasc Surg 1986;91:924–8.
6. Tsai TP, Matloff JM, Chaux A, et al. Combined valve and coronary artery bypass procedures in septuagenarians and octogenarians: results in 120 patients. Ann Thorac Surg 1986;42:681–4.
7. Edmunds LH, Stephenson LW, Edie RN, et al. Open-heart surgery in octogenarians. N Engl J Med 1988;319:131–5.
8. Rich MW, Sandza JG, Kleiger RE, et al. Cardiac operations in patients over 80 years of age. J Thorac Cardiovasc Surg 1985;90:56–60.
9. Goldman BS, Scully HE, Tong CP, et al. Coronary artery bypass (CAB) in the elderly. Circulation 1987;76(Suppl 4):352.
10. Dorros G, Lewin RF, Daley P, et al. Coronary artery bypass surgery in the geriatric population. Circulation 1987;76(Suppl 4):486.
11. Acinapura AJ, Rose DM, Cunningham JN, et al. Coronary artery bypass in septuagenarians: analysis of mortality and morbidity. Circulation 1987;76(Suppl 4):353.
12. Freeman WK, Tajik AJ, Schaff HB, et al. Cardiac surgery in patients 80 years and older: early and late postoperative results. Circulation 1987;76(Suppl 4):390.
13. Elayda MA, Hall RJ, Gray AG, et al. Coronary revascularization in the elderly patient. J Am Coll Cardiol 1984;3:1398–402.
14. Berry BE, Acrec PW, Davis PJ, et al. Coronary artery bypass operation in septuagenarians. Ann Thorac Surg 1981;31:310–3.
15. Gersh BJ, Schaff HV, Kronmal R, et al. Bypass for the elderly—a CASS registry update. Cardiovasc Med 1984;Nov:890–7.
16. Ennabli K, Pelletier L. Morbidity and mortality of coronary artery surgery after the age of 70 years. Ann Thorac Surg 1986;42:197–200.
17. Roberts AJ, Woodhall DD. Mortality, morbidity and cost-accounting related to coronary artery bypass graft surgery in the elderly. Ann Thorac Surg 1985;39:426–32.
18. Rose DM, Gelbfish J, Jacobowitz IJ, et al. Analysis of morbidity and mortality in patients 70 years of age and over undergoing isolated coronary artery bypass surgery. Am Heart J 1985;110:341–6.
19. Johnson WD, Gessert RJ, Brenowitz JB, et al. Complex cardiovascular surgery in the geriatric population. Circulation 1987;76(Suppl 4):486.
20. Loop FD, Lytle BW, Cosgrove DM, et al. Coronary artery bypass graft surgery in the elderly. Cleve Clin J Med 1988;55:23–4.
21. Tsai TP, Chaux A, Matloff JM. Aortocoronary bypass surgery in septuagenarians and octogenarians. J Cardiovasc Surg 1989;30:364–8.
22. BMDP statistical software. Los Angeles: University of California Press, 1985.
23. Kuan P, Bernstein SB, Ellestad MH, et al. Coronary artery bypass surgery morbidity. J Am Coll Cardiol 1984;3:1391–7.
24. Acinapura AJ, Rose DM, Cunningham JN, et al. Coronary artery bypass in septuagenarians. Analysis of mortality and morbidity. Circulation 1988;78(Suppl 1):179.

Heterotopic Heart Transplantation and Native Heart Ventricular Arrhythmias

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Heterotopic heart transplantation has been said to be contraindicated in patients with serious native heart arrhythmias that produce hemodynamic instability. Placement of heterotopic allografts, however, can theoretically act as a biological biventricular assist device to provide hemodynamic support during these unstable rhythms. Further, this operation might beneficially alter the hemodynamic milieu of heart failure such that the arrhythmias are ameliorated. Described is our experience with 4 patients with heart failure receiving heterotopic cardiac allografts, documenting changes in native heart arrhythmia that occurred. These cases demonstrate that heterotopic grafts can adequately sustain hemodynamics during malignant native heart dysrhythmia. We believe native heart ventricular arrhythmias are not a contraindication to heterotopic heart transplantation.

(Ann Thorac Surg 1991;51:987–91)

Cardiac transplantation for end-stage heart disease is a well-accepted treatment modality, but there continues to be a serious mismatch between the number of patients who require transplantation and the number of donor organs available [1–3]. During this waiting period, many patients die of sudden cardiac death and heart failure [4–6]. In an attempt to more efficiently use scarce donors and shorten pretransplantation waiting time, heterotopic transplantation has recently been reinstituted at our institution, the primary indication being donor-recipient size mismatch. Previously, reports suggested that native heart ventricular dysrhythmias were a contraindication to placement of an allograft in the heterotopic position because these arrhythmias may cause symptoms of low cardiac output and allow the formation of left ventricular thrombi [7, 8].

Theoretically, by improving heart failure patients' overall hemodynamics with heterotopic transplantation, the consequences of native heart ventricular dysrhythmias might be ameliorated and, in some patients, the arrhythmia itself eliminated. This report details 4 male patients with severe left ventricular dysfunction who received heterotopic heart transplants because of availability of small donors only. The changes in native heart ventricular dysrhythmias after heterotopic transplantation and revascularization are described.

Material and Methods

Presently patients being considered for heterotopic cardiac transplantation are required to have not undergone a previous cardiac operation. Preparation for cardiopulmonary bypass is done by placing the aortic cannula as far distal in the ascending aorta as is practical; venocaval cannulation is accomplished high on the right atrial wall. A partial occluding clamp is applied to the pulmonary artery and an 18- to 22-mm preclotted, woven Dacron graft is sewn end to side to the pulmonary artery; should hemodynamic instability result, cardiopulmonary bypass is instituted. In patients who underwent concomitant coronary artery bypass, cardioplegia was delivered retrograde through a transatrial cannula inserted blindly into the coronary sinus. The bypass procedure was timed so that the distal anastomosis was completed at the time of arrival of the donor heart.

The remainder of the procedure is very similar to that described by Novitzky and associates [9], with left atria anastomosed side to side; superior vena cava, end to side; aorta, end to side; and pulmonary artery, side to end to the previously placed graft. This last anastomosis is performed after release of the aortic cross-clamp. Both ventricles are aspirated for air, and both aortas are vented for air. Proximal coronary anastomoses are then sewn onto the donor aorta. Temporary pacing wires are placed on both right ventricular free walls and both hearts are cardioverted if necessary.

Patient 1

A 56-year-old man with ischemic heart disease and previous myocardial infarction resulting in an ejection fraction less than 0.20 was referred for cardiac transplantation. A pretransplantation ambulatory electrocardiographic monitoring study demonstrated frequent multiform ventricular premature beats and runs of nonsustained ventricular tachycardia with the longest being eight beats. Owing to the patient's worsening condition, heterotopic transplantation

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Table 1. Hemodynamic Variables Before and After Heterotopic Transplantation[a]

	Patient 1		Patient 2		Patient 3		Patient 4	
Variable	Before	After	Before	After	Before	After	Before	After
LVEF	0.15	. . .	0.24	. . .	0.22	. . .	0.20	. . .
RA (native) (mm Hg)	11	4	20	8	17	6	22	4
RV (native) (mm Hg)	50/11	44/4	35/10	28/8	43/17	30/6	40/20	28/4
PA (mm Hg)	50/34	40/8	38/20	28/20	43/23	27/17	45/24	42/20
PCW (mm Hg)	22	13	20	12	23	14	19	15
Ao (mm Hg)	98/60	100/60	90/50	124/84	88/54	132/94	102/58	140/98

[a] Intracardiac pressures represent those measured in the native heart.

Ao = aortic pressure (systolic/diastolic); LVEF = left ventricular ejection fraction; PA = pulmonary artery pressure (systolic/diastolic); PCW = pulmonary capillary wedge pressure; RA = right atrial pressure; RV = right ventricular pressure (systolic/end-diastolic).

was considered to attenuate any prolongation of the waiting period. A small donor of appropriate blood group became available (recipient weight, 67.5 kg; donor weight, 39.6 kg), and transplantation was performed. The operative procedure was unremarkable. In addition to the transplantation, the patient had aortocoronary bypass grafts placed to the left anterior descending and obtuse marginal coronary arteries of the native heart at the time of operation.

Postoperatively the patient experienced normal recovery until the sixth day, when atrial fibrillation of the implanted donor heart developed; it was successfully treated with digoxin. On the eighth postoperative day 20 seconds of a wide complex tachycardia was detected during monitoring of his native heart. At that time his electrolyte levels were normal and he was asymptomatic. Cardiac monitoring was continued and approximately 3 days later another run of sustained ventricular tachycardia was observed. The patient noted weakness at the onset of the dysrhythmia and, for this reason, was started on a regimen of oral procainamide. He had no further episodes of ventricular tachycardia while in the hospital, and none was detected during 48-hour ambulatory monitoring 4 weeks after transplantation.

He returned to home and work in excellent condition, but 6 weeks later symptoms of mild exercise intolerance developed. His local physician noted native heart sustained ventricular tachycardia on an electrocardiogram. Antiarrhythmic drug levels were obtained and the procainamide and *n*-acetylprocainamide levels were subtherapeutic. Because the patient had minimal symptoms and was on systemic anticoagulation, no cardioversion was undertaken despite continuous native heart ventricular tachycardia. Rather, the procainamide dosage was increased and the patient was seen again in clinic 3 days later. At that time, his native heart had converted to normal sinus rhythm, and the symptoms were gone. The patient has subsequently had no further known episodes of ventricular dysrhythmia and has continued to feel well. Table 1 summarizes selected hemodynamics before and after operation.

Patient 2

Patient 2 is a 58-year-old man with idiopathic dilated cardiomyopathy, severe ventricular ectopy, and sudden cardiac death on two occasions. He had been receiving encainide for treatment of his arrhythmia. His symptoms were of New York Heart Association class IV heart failure. His ejection fraction was less than 0.20 (see Table 1). Heterotopic transplantation was performed because of clinical instability and frequent episodes of sustained ventricular tachycardia on ambulatory electrocardiographic monitoring. A small donor was used for this patient (recipient weight, 94.5 kg; donor weight 60.8 kg). In the early postoperative period atrial fibrillation developed with a rapid ventricular response noted in the native heart (rate, 170 beats/min). This arrhythmia was hemodynamically insignificant and rate control was obtained easily with intravenous digoxin therapy.

One acute rejection episode occurring early after transplantation was managed with steroids and OKT3 per protocol [2]. After this therapy, the level of rejection decreased and no further episodes occurred. Both hearts remained in sinus rhythm, and he was discharged home in excellent condition and receiving no antiarrhythmic medication. Throughout the 10 months after his heterotopic transplantation the patient has had no further syncope or exercise intolerance, and multiple ambulatory electrocardiographic monitorings have demonstrated only rare ventricular premature beats and no runs of ventricular tachycardia.

Patient 3

Patient 3 is a 47-year-old man who had recently suffered a large anterior wall myocardial infarction complicated by ventricular fibrillation and cardiogenic shock requiring the placement of an intraaortic balloon pump. His ejection fraction determined on maximal inotropic support was 0.22 (see Table 1). Throughout the waiting period his functional status was New York Heart Association class IV on maximal inotropic support. He continued to have runs of nonsustained ventricular tachycardia and occasional episodes of sustained ventricular tachycardia requiring therapy with parenteral procainamide. An organ became available that was suitable for heterotopic transplantation (recipient weight, 83.3 kg; donor weight, 48.6 kg) and was accepted because of the patient's precarious status. During operation, he also underwent coronary bypass grafting to the left anterior descending and right coronary arteries of the native heart.

On the tenth postoperative day native heart ventricular tachycardia again developed. The patient remained hemodynamically stable and was unaware of this rhythm. Procainamide levels at the time were found to be therapeutic and attempts were made to electrically cardiovert the heart. These attempts were unsuccessful, and procainamide administration was therefore stopped and quinidine administration begun along with systemic anticoagulation to prevent thrombus formation in the native heart. Two days later the native heart spontaneously converted to normal sinus rhythm. One month after discharge malaise, arthralgia, nausea, diarrhea, and a skin rash developed. These symptoms were believed to be related to the quinidine therapy. Administration of the antiarrhythmic was stopped, and it was not replaced because the rhythm was previously well tolerated. In the 8 subsequent months he has had no recurrence of any serious arrhythmia. Ambulatory monitoring demonstrates multiform native heart premature ventricular contractions but no episodes of ventricular tachycardia.

Patient 4

The final patient is a 46-year-old man weighing 103.5 kg with coronary artery disease and congestive heart failure. He had symptomatic ventricular tachycardia occurring after a large myocardial infarction. Antiarrhythmic agents would no longer control his ventricular dysrhythmia and he had several episodes of sustained ventricular tachycardia that could not be easily cardioverted. Electrophysiologic testing failed to identify a drug that would prevent induction of ventricular tachycardia or substantially alter the cycle length. Because of the frequency of the arrhythmia and difficulty with electrical cardioversion, an implantable defibrillator could not be used. In light of progressive heart failure symptoms, abnormal hemodynamics (see Table 1), and serious ventricular arrhythmia, the patient was believed to be a transplantation candidate.

A donor organ became available (donor weight, 56.7 kg) that was suitable for heterotopic transplantation. We anticipated the procedure would improve his cardiac hemodynamics and eliminate the ventricular tachycardia; or, if the organ was undersized, the operation could be the first step in a staged procedure, potentially resulting in placement of a second donor organ. At the time of operation, sapheneous vein coronary bypass grafts were placed to the obtuse-marginal coronary artery and to the circumflex coronary artery.

On the second postoperative day, sustained ventricular tachycardia that was resistant to therapy with procainamide again developed in his native heart. The patient noted only exertional dyspnea. With the circulatory protection provided by the donor heart, mapping of the native heart and catheter ablation of the ventricular tachycardia foci was electively attempted but unsuccessful. The native heart arrhythmia progressed to ventricular fibrillation (Fig 1). Direct-current conversion caused the native heart to revert to ventricular tachycardia and again the patient had only exertional dyspnea. Though the patient's condition gradually improved, no substantive increase in exercise tolerance could be achieved. Another small donor organ (donor weight, 51.8 kg) became available that was believed suitable for orthotopic implantation, leaving the heterotopic heart untouched. After the procedure the patient had no further symptoms and was discharged in excellent condition. He has had no further episodes of arrhythmia in either heart.

Comment

It should be pointed out that, as a group, these patients had meticulous management of their metabolic variables and hemodynamic status both before and after transplantation in an effort to control, treat, or prevent dysrhythmias.

These cases represent the varied responses of native heart ventricular arrhythmias to heterotopic transplantation. This small series represents greater than 20% of the heterotopic transplantation done during this time period [10], and suggests that the notion ventricular arrhythmias are an absolute contraindication to heterotopic transplantation needs reconsideration. In 1 patient, the arrhythmia that had caused sudden cardiac death completely resolved with no concomitant antiarrhythmic therapy. In another patient, the arrhythmia persisted early on, but as donor heart function improved, the patient was able to be weaned from antiarrhythmic medications, and since then there have been no further episodes of ventricular dysrhythmia. In the third patient, nonsustained ventricular tachycardia noted preoperatively evolved to sustained ventricular tachycardia after transplantation but was hemodynamically insignificant and manifested only as mild exercise intolerance. This rhythm could then be easily treated on an outpatient basis with oral procainamide while the donor heart sustained circulation, operating as a biological biventricular assist device. Finally, there is the patient in whom ventricular dysrhythmias could not be corrected with heterotopic transplantation, but the procedure offered a therapeutic bridge to a more definitive operation, creating hemodynamic stability despite malignant arrhythmias in his native heart. Although left ventricular thrombus may occur in these patients, a stable rhythm and systemic anticoagulation should prevent this.

Sustained ventricular tachycardia and resultant sudden cardiac death now appears to be one of the main causes of death in patients with end-stage cardiac failure, particularly in patients with ischemic heart disease. The Cardiac Arrhythmia Suppression Trial and other reports have demonstrated that treatment of this type of patient with class IC agents may actually be harmful [11, 12]. Furthermore, the administration of certain antiarrhythmic agents to patients with the triad of depressed ejection fraction, ischemic heart disease, and nonsustained ventricular tachycardia is detrimental [12]. Because of elevated end-diastolic pressures, increased plasma catecholamine levels, and frequent electrolyte abnormalities (particularly potassium and magnesium depletion), patients with terminal cardiac dysfunction are very prone to ventricular dysrhythmia and sudden death syndrome [13]. Possibly,

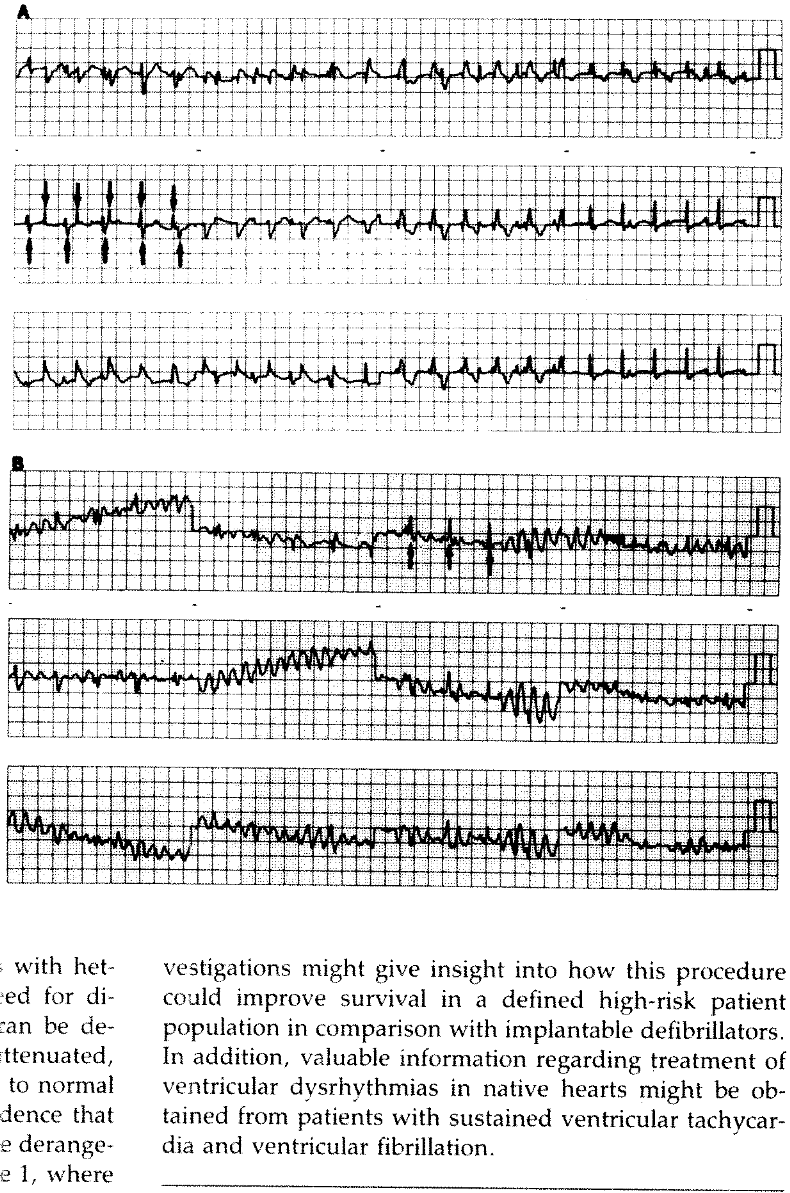

Fig 1. (A) Twelve-lead electrocardiogram of patient 4. Arrows show two distinct complexes; top arrows represent the heterotopic heart. (B) The same patient with native heart ventricular fibrillation. Arrows show donor heart complexes still clearly seen in the right precordial leads. Hemodynamically, the patient was stable during this arrhythmia.

by correcting the hemodynamic abnormalities with heterotopic transplantation and lowering the need for diuretic therapy, plasma catecholamine levels can be decreased and metabolic derangements can be attenuated, thus creating an environment more conducive to normal sinus rhythm in the native heart [14, 15]. Evidence that heterotopic implants can attenuate at least some derangements due to heart failure is presented in Table 1, where hemodynamics in these 4 patients before and after heterotopic transplantation are summarized. As can be seen, the classic heart failure hemodynamics have been improved after operation.

We conclude that heterotopic transplantation is not absolutely contraindicated in the face of severe ventricular dysrhythmia as has been previously suggested. This procedure is a viable option in a select group of patients in whom ventricular dysrhythmias occur in the presence of severe cardiac dysfunction. Certainly orthotopic transplantation is the procedure of choice in many of these patients; however, because of the constraints of donor availability, heterotopic transplantation becomes a more attractive option, particularly in light of the fact that survival of patients receiving heterotopic transplants in recent years is approaching the survival of their orthotopic counterparts [14], and most patients who die awaiting transplantation succumb to sudden cardiac death. Further studies evaluating arrhythmias after heterotopic transplantation in quantitative fashion are needed. These investigations might give insight into how this procedure could improve survival in a defined high-risk patient population in comparison with implantable defibrillators. In addition, valuable information regarding treatment of ventricular dysrhythmias in native hearts might be obtained from patients with sustained ventricular tachycardia and ventricular fibrillation.

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References

1. Evans RG, Mannimen DC, Gersh BJ, et al. The need for and supply of donor hearts for transplantation. Heart Transplant 1984;4:57–60.
2. Young JB, Leon CA, Lawrence EC, et al. Heart replacement for terminal cardiac disease: cardiac transplantation and mechanical sustenance of the cardiovascular system. Parts I and II. Baylor Cardiology Series 1989;12(3):4–27; 1989;12(4): 4–27.
3. Copeland JG, Emery PW, Levinson MM, et al. Selection of patients for cardiac transplantation. Circulation 1987;75:2–9.
4. Follansbee WP, Michelson EL, Morganroth J. Nonsustained ventricular tachycardia in ambulatory patients: characteristics and association with sudden cardiac death. Ann Intern Med 1980;92:741–7.

5. McKee PA, Castelli WP, McNamera PM, et al. The natural history of congestive heart failure. The Framingham Study. N Engl J Med 1971;285:1441–5.
6. Fowler MB, Schroeder JS. Current status of cardiac transplantation. Mod Concepts Cardiovasc Dis 1986;55:37–41.
7. Cooper DKC, Novitzky D, Becerra E, Reichart B. Are there indications for heterotopic heart transplantation in 1986? Thorac Cardiovasc Surg 1986;34:300–4.
8. Kennelly BM, Corte P, Losman J, Barnard CN. Arrhythmias in two patients with left ventricular bypass transplants. Br Heart J 1976;38:725–31.
9. Novitzky D, Cooper D, Barnard C. The surgical technique of heterotopic heart transplantation. Ann Thorac Surg 1983;36:476–82.
10. Kriett JM, Kaye MP. The Registry of the International Society for Heart Transplantation: Seventh Official Report—1990. J Heart Transplant 1990;9:323–30.
11. Cardiac Arrhythmia Suppression Trial (CAST) investigators. Effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. N Engl J Med 1989;321:406–12.
12. Pratt CM, Eaton T, Francis M, et al. The inverse relationship between baseline left ventricular ejection fraction and outcome of antiarrhythmic therapy: a dangerous imbalance in the risk-benefit ratio. Am Heart J 1989;118:433–40.
13. Unverferth DV, Magorien RD, Moeschberger ML, Baker PB, Fetters JK, Leier CV. Factors influencing the one-year mortality of dilated cardiomyopathy. Am J Cardiol 1984;54:147–52.
14. Kawaguchi A, Gandjbakhch I, Pavie A, et al. Factors affecting survival after heterotopic heart transplantation. J Thorac Cardiovasc Surg 1989;98:928–34.
15. Raza ST, Tam SKC, Sun S-C, et al. Sequentially paced heterotopic heart transplant in the left chest provides improved circulatory support for the failed left ventricle. J Thorac Cardiovasc Surg 1989;98:266–74.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1994 may begin the recertification process in 1992. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is May 1, 1992. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

New Technique for Pacemaker Implantation in the Upper Chest of Children and Women

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A new lateral approach for implanting pacemaker generators in the chest of women and children is described. Using this technique, 83 women and 21 children were operated on with no early or late complications and with good cosmetic results up to 9 years after operation. This technique prevents formation of visible wide scars above the breast in women and prevents thinning or disruption of the chest incision in children. Ages of the women ranged from 19 to 56 years; children, 5 to 18 years. In 23 patients, this technique was used after wound complications had occurred 7 days to 3 years after use of the standard implantation technique.

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The standard technique for implanting transvenous pacemaker systems involves an incision in the subclavicular area where the pacemaker pocket is created and the pulse generator implanted. In the adult patient, this technique involves very little deformity or inconvenience, except that the battery sometimes is too close to the axilla and may interfere with the patient's occupation or activity.

Dehiscence of the incision with infection is rare, but can happen, most commonly due to the large size and pressure of the pulse generator. It is particularly so if the battery is placed in an area of excessive mobility.

In women, and in children 5 to 18 years old, however, an incision in this chest area is highly undesirable. In women, an incision in the front of the chest is undesirable because of the cosmetic implications either above or below the clavicle, particularly if complications occur. One important factor is the weight of the breast. The constant stretching of the skin affects any incision placed transversely between the clavicle and the breast. In children, the subcutaneous layer in the chest is usually thin. Even when the incision heals, the scar becomes thin and wide with time owing to gradual separation of the subdermic layers.

To avoid these problems in women and children undergoing implantation of transvenous pacemaker systems, I developed a new technique, a lateral approach for implanting the pulse generator that can easily be done under local or general anesthesia. It hides the incision behind the breast and is not visible when the arm is down. I now prefer this new technique when implanting transvenous pacemaker units in women and children.

Material and Methods

Patients

Between 1980 and 1990, 83 women and 21 children underwent operation at the University of Minnesota Hospital and Clinic using this technique. The age of the women varied from 19 to 56 years; children, 5 to 18 years. Owing to complications at the pulse generator site, 23 patients were referred from outside institutions with infections, deforming scars, or erosion. All 23 patients were treated by implantation of a new pulse generator and leads on the opposite side using the lateral approach. No attempts were made to resterilize the removed unit. In 12 patients, it was possible to remove the old leads completely. In the remaining 11 patients, only partial removal was accomplished.

Operative Technique

The patient is positioned flat on the operating table, with the right side of the chest slightly elevated to 15 degrees. The arm is abducted slightly toward the edge of the table, while the rest of the body is moved to the opposite side. The incision is made in the lateral groove of the breast or lateral fold of the pectoralis major (Fig 1). The site is marked preoperatively with the patient in the sitting-up position (the best way to assess where the scar will not be visible and not interfere with clothing). After the subcutaneous tissue is entered, the lateral border of the pectoralis major muscle is reached. The dissection is carried anteriorly to the muscle and medially toward the anterior wall of the chest. The aim is to have the center of the pocket about 5 cm from the midline anteriorly and 10 cm from the clavicle in the adult patient, or the equivalent in a child.

The pocket is created under the subcutaneous tissue. Once the pacemaker leads are implanted through percutaneous puncture of the subclavian vein, a small incision is made at that level, which allows maneuvering the lead to tunnel it down into the future pulse-generator pocket. The pulse generator is then connected and positioned into

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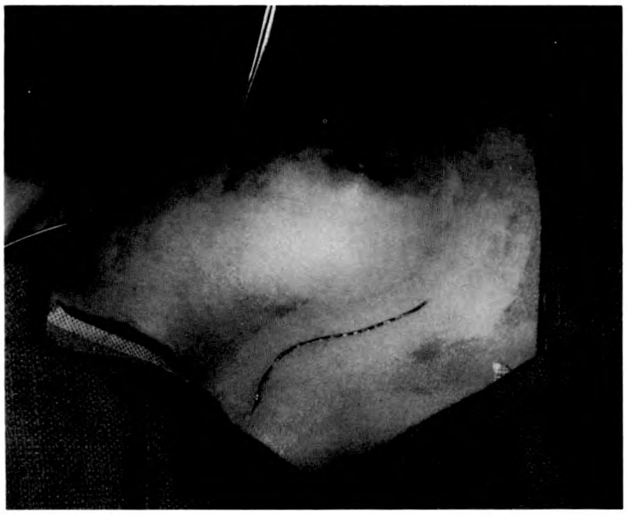


Fig 1. Site of the incision for the lateral approach of pacemaker implantation. In the left-hand corner, the pacemaker lead already inserted in the subclavian vein can be seen. The forceps point to the area where the pulse generator will be located.

the pocket. Two or three interrupted stitches with absorbable material are placed between the anterior fascia of the pectoralis major and the posterior subcutaneous fascia. This is important to prevent migration of the battery pack laterally toward the axilla. It is preferable, in general, to place the pulse generator far medially rather than laterally. The subcutaneous tissue is then closed with nonabsorbable material and the skin approximated in the preferred manner. Steri-strips (3-M Co, St. Paul, MN) are mostly used instead of sutures or staples. Patients are usually discharged the next day and then followed up in the outpatient clinic.

Results

This new technique has met with wide acceptance and satisfaction by the patients. The follow-up period extends from 6 months to 9 years, during which no reoperation has been required for repositioning of the unit or for incision-related complications. No migrations or infections of the pacemaker system have occurred. The pulse generator has been replaced at the end of the battery lifespan in 9 patients, using the same approach, without any problems.

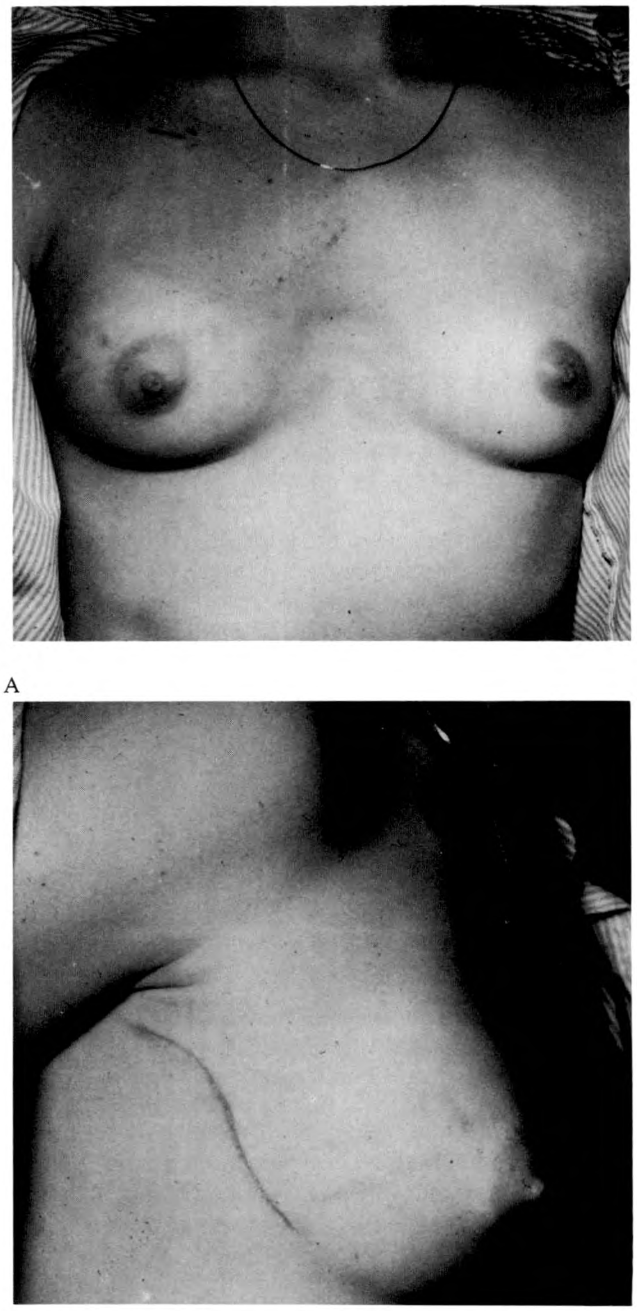
The cosmetic results have been excellent (Fig 2), particularly when the pacemaker pulse generators are small. Even when the pacemaker units are large proportionate to the size of the patient, no sensitive spots have developed over the generator site as are frequently seen when the battery is buried directly under a surgical incision.

Experience in Women

In 83 women, lateral pulse generator implantations (78 transvenous, 5 epicardial) were done. In the transvenous group, 30 women required single-chamber implants in the ventricle; 48, dual-chamber. Indications for placing epicardial leads were thrombosis of the superior vena cava (1), single ventricle (1), presence of tricuspid valve prosthesis (2), and after a Fontan operation (1).

Experience in Children

Of the 21 children, 10 had congenital heart block associated with intracardiac anomalies. The other 11 had complications from intracardiac surgical correction of defects



A

B

Fig 2. Late results of the lateral approach in a 23-year-old woman with congenital heart block, using the lateral approach shown in Figure 1. (A) Front view with no visible deforming scar. (B) Lateral view showing complete healing of the incision, causing no deformity.

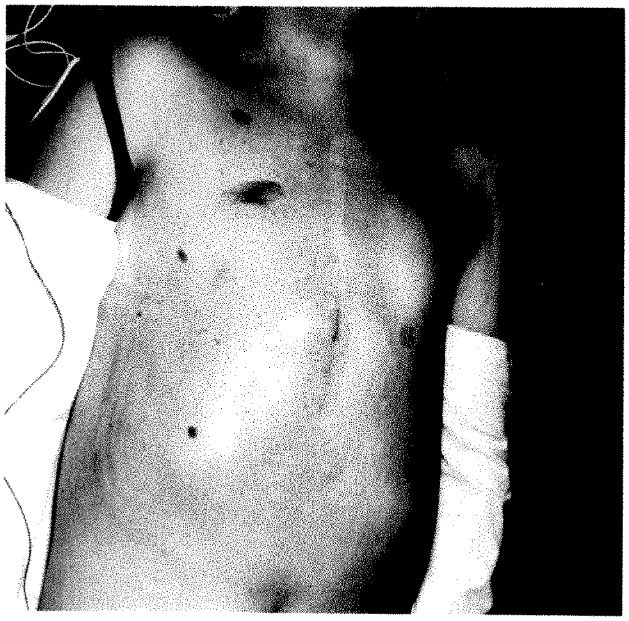


Fig 3. *Ten-year-old boy who had pacemaker implanted originally on the right side of the chest, which led to dehiscence of the transverse incision over the pectoral area and infection requiring removal of the entire system. The illustration also shows the final result of implanting the same-size unit on the opposite side using the lateral approach.*

performed at various times by several surgeons. All 10 cases of congenital heart block were treated with implantation of dual-chamber pacemaker systems. In the group with postsurgical heart block, 5 required a single-chamber (ventricle) system; 6, a dual-chamber. Two children had pacemakers previously implanted using the standard technique with an incision in the front of the chest, which led to erosion and dehiscence of the incision with infection as late as 2 months after implantation. These complications required removal of the entire pacemaker system and reimplantation of a new one in the opposite side (Fig 3); no subsequent complications were experienced 5 and 8 years after reimplantation.

Comments

Implanting transvenous pacemaker systems in children must fulfill several requirements. The pacemaker lead should be small enough so it can be safely introduced in the subclavian vein without causing obstruction to the venous flow or thrombosis from damaging the intima. The lead should also be long enough but not excessively redundant that the remaining portion outside the vein must be wrapped around the pacemaker generator causing undesirable bulk. Because of these considerations, at our institution we have not attempted to place transvenous pacemaker systems in the chests of children younger than 5 years old.

Holmes and associates [1] at the Mayo Clinic reported 1 case of placing the catheter in the subclavian vein of an 18-month-old patient with success. However, late follow-up results are not available concerning the pulse-generator site in such a small infant. Furman and Young [2] reported 13 transvenous implants in children but did not state what problems they experienced at the pulse-generator implant site. Of 19 children who received both epicardial and transvenous systems, only 2 did not require reoperation within 2 years after implantation. The report did not specify whether the pulse generators were implanted in the chest or the abdomen. Whitman and colleagues [3] reported 9 patients less than 18 years old with pacemaker implants, but did not specify how many were transvenous or epicardial systems. Siddons [4] reported 11 cases of transvenous implants in children. Hayes and co-workers [5] reported implantations in older children through the transvenous route but gave no details on the outcome or complications.

Because of the disadvantages of an epicardial system, with its high lead failure rate [6–8], the current tendency in older children is to implant a transvenous system as early as feasible. However, the transvenous technique implies a pulse generator implant in the chest. This may not be ideal in small children because they have a very thin subcutaneous layer and the pacemaker generator becomes too bulky, exerting substantial tension on the surgical incision. Although the current single-chamber pulse generators are small and thin, the use of dual-chamber systems (with or without rate-responsive capabilities) entails a larger unit. In the report by Ward and associates [9] of transvenous pacemaker implantations in children less than 10 kg, 1 out of 5 children experienced erosion of the system; it is not mentioned whether the pulse generator was implanted in the abdomen or the chest.

In 1988, Walsh and co-workers [10] described implanting 27 of 39 pacemakers in children using the transvenous route. However, only 13 pulse generators were implanted in the chest. In the entire group of 39 patients, only 4 infections (10%) occurred. It is not clear where the infections were located.

In women, the inframammary approach described by Belott and Bucko [11] is cosmetically well accepted. However, in children or adolescents, the location of this groove is not predictable. Often, incisions made in the chest migrate when the child grows and end up being across the breast instead of in the inframammary groove. In older women with pendulous breasts, the inframammary groove is not a desirable location for an incision owing to the risk of skin maceration, poor healing, and infection. For those reasons, the inframammary approach was avoided in the group of patients reported here, but it does constitute another acceptable technique in young women.

One factor leading to wide scar formation in women is separation of the skin edges or of the dermic layer caused by the weight of the breast. If dehiscence or infection occurs, the results may be devastating.

For a period of up to 9 years of follow-up, we have seen no complications related to the technique employed. The cosmetic results have been highly satisfactory and acceptable to the patients. Therefore, I recommend the lateral approach. Tension over the pulse generator is minimal, and there is no incision over it.

Although the lateral approach was designed specifically for women and children, it can also be used in any adult patient who has thin subcutaneous layers over the chest wall.

References

1. Holmes DR, Maloney JD, Feldt RH. The use of the percutaneous subclavian technique for permanent cardiac pacing in childhood. Mayo Clin Proc 1980;55:579-82.
2. Furman S, Young D. Cardiac pacing in children and adolescents. Am J Cardiol 1977;39:550-8.
3. Whitman V, Berman W Jr, Tyers GFO. Pacemakers in young patients. J Pediatr 1978;92:722-4.
4. Siddons H. Transvenous pacing in the child. Ann Cardiol Angiol 1971;20:445-7.
5. Hayes DL, Holmes DR Jr, Mahoney JD, et al. Permanent endocardial pacing in pediatric patients. J Thorac Cardiovasc Surg 1983;85:618-24.
6. Simon AB, Dick M, Stern AM, Behrendt DM, Sloan H. Ventricular pacing in children. PACE 1982;5:836-44.
7. Williams WG, Izukawa T, Olley PM. Permanent pacing in infants and children. PACE 1978;1:439-44.
8. Young D. Permanent pacemaker implantations in children: current status and future considerations. PACE 1981;4:61-7.
9. Ward DE, Jones S, Shinebourne EA. Long-term transvenous pacing in children weighing less than 10 kg [Abstract]. Circulation 1985;(Suppl 3):72.
10. Walsh C, McAlister H, Andrews C, Steeg C, Eisenberg R, Furman S. Evolution of pacemaker implantation technique in children [Abstract]. PACE 1988;11:483.
11. Belott PH, Bucko D. Inframammary pulse generator placement for maximizing cosmetic effect. PACE 1983;6:1241-4.

Notice From the Southern Thoracic Surgical Association

The Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Hyatt Regency Grand Cypress, Orlando, Florida, November 7-9, 1991. There will be a $250 registration fee for nonmember physicians except for guest speakers, authors and coauthors on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 7, 1991. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Members wishing to participate in the Scientific Program should submit an original abstract and one copy by May 15, 1991, to Frederick L. Grover, MD, Program Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267. Abstracts must be submitted on the Southern Thoracic Surgical Association abstract submission form. These forms may be obtained from the Association's office or in the April issue of *The Annals of Thoracic Surgery*. All slides used during the presentation must be 35 mm. Manuscripts of accepted papers must be submitted to *The Annals of Thoracic Surgery* prior to the 1991 meeting or to the Secretary-Treasurer at the opening of the Scientific Session.

Applications for membership should be completed by July 1, 1991, and forwarded to F. Hammond Cole, Jr, MD, Membership Committee Chairman, Southern Thoracic Surgical Association, 401 North Michigan Avenue, Chicago, IL 60611-4267.

Hendrick B. Barner, MD
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Sinus of Valsalva Aneurysm Eroding Into the Interventricular Septum

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Abdool Aniff Sorefan, FRCS, and Mohamed Taher Kayali, FRCS

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We report a case of erosion of an aneurysm of the right sinus of Valsalva into the interventricular septum. The mode of presentation, the preoperative evaluation, and the echocardiographic and nuclear magnetic resonance imaging features are presented, and the cardiac catheterization findings and surgical management of this very rare cardiac pathology are discussed.

(Ann Thorac Surg 1991;51:996–8)

Aneurysms of the sinuses of Valsalva account for about 0.34% of all cases submitted to open heart operation [1]. Rupture of these aneurysms into adjacent structures is a well-recognized complication. It is extremely rare for the interventricular septum to harbor such an aneurysm [2]. These aneurysms are predominantly of congenital origin. Other etiological factors documented are bacterial endocarditis, trauma, dissection of the aorta, rheumatoid arthritis, Marfan's syndrome, and atherosclerotic degeneration. Mural connective tissue degeneration results in weakening of the sinuses, which eventually give way under the constant hammering of the aortic pressure head [3]. Apparently, Orientals are more prone to the development of these aneurysms [4].

A 30-year-old woman had a 3-month history of sudden onset palpitation and effort intolerance culminating in heart failure. Cardiac auscultation revealed a grade 2/6 diastolic murmur along the left sternal border. Electrocardiography revealed sinus bradycardia and right bundle-branch block. M-mode and two-dimensional echocardiography revealed the presence of a large cyst in the interventricular septum in the subaortic region (Fig 1). Nuclear magnetic resonance imaging proved useful in the diagnosis and clearly depicted the aneurysmal sac (Fig 2). Cardiac echinococcosis deserves consideration in our patient population; however, all serological tests for this condition were negative. Cardiac catheterization revealed normal intracardiac pressures and saturations. The coronary arteries were normal. Aortic root angiography showed opacification of the interventricular pouch and established its origin from the right coronary sinus. There was no communication with the ventricles. The pouch bulged into the right ventricle during systole (Fig 3).

The patient underwent an open heart operation using cardiopulmonary bypass and cold crystalloid cardioplegia. An oblique aortotomy provided good exposure. A defect of 1 cm^2 was present in the floor of the right coronary sinus. This led into a large aneurysmal sac (5 × 3 cm) with a smooth endocardial lining located in the subaortic region of the septum. The noncoronary and left coronary sinuses were normal. The defect in the floor of the right coronary sinus was patched with autologous pericardium. The patient was easily weaned off bypass. However, the occurrence of a persistent complete atrioventricular block necessitated placement of a permanent pacemaker. The patient is now doing well, has no signs of heart failure, and has good exercise tolerance with a follow-up of 27 months.

Comment

Aneurysms of the sinuses of Valsalva occur rarely. The right sinus, the noncoronary sinus, and the left sinus are affected in decreasing order of frequency. Rupture of the aneurysms into a cardiac chamber is a well-recognized phenomenon [5]. Aneurysms of the right sinus of Valsalva tend to rupture into the right ventricle [3]. This entity is often associated with a ventricular septal defect. Erosion into the interventricular septum is the rarest complication.

The condition may manifest itself gradually or suddenly, or it may remain asymptomatic. Our patient was in heart failure when first seen. This was probably caused by obstruction of the outflow tract of both ventricles by the bulging aneurysmal sac and was presumably precipitated by the development of arrhythmias as the patient's condition was heralded by palpitation. Our patient had right bundle-branch block preoperatively. This conceivably resulted from pressure on the conduction tissue by the tense aneurysmal pouch. Complete heart block attributed to unruptured aneurysm of the sinus of Valsalva has been reported [6]. Anatomical distortion caused by the expanding aneurysmal pouch renders the conduction tissues particularly vulnerable during operation. The presence of conduction disturbances in association with a cystic mass in the interventricular septum on echocardiography should hint at the diagnosis. Nuclear magnetic resonance imaging proved valuable in delineating the cystic mass. Cardiac catheterization and cineangiography serve to es-

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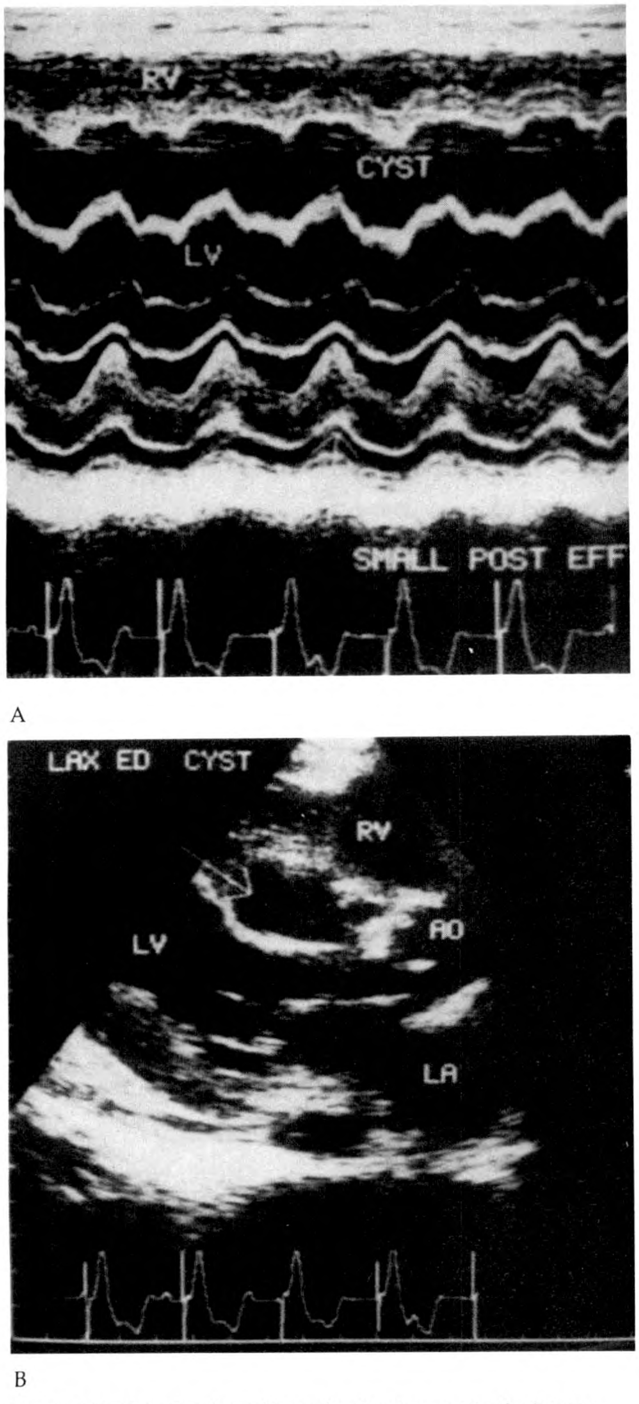

Fig 1. (A) M-mode echocardiography showing cyst in the interventricular septum. (B) Two-dimensional echocardiography showing cyst into the interventricular septum. (AO = *aorta;* LA = *left atrium;* LV = *left ventricle;* RV = *right ventricle.)*

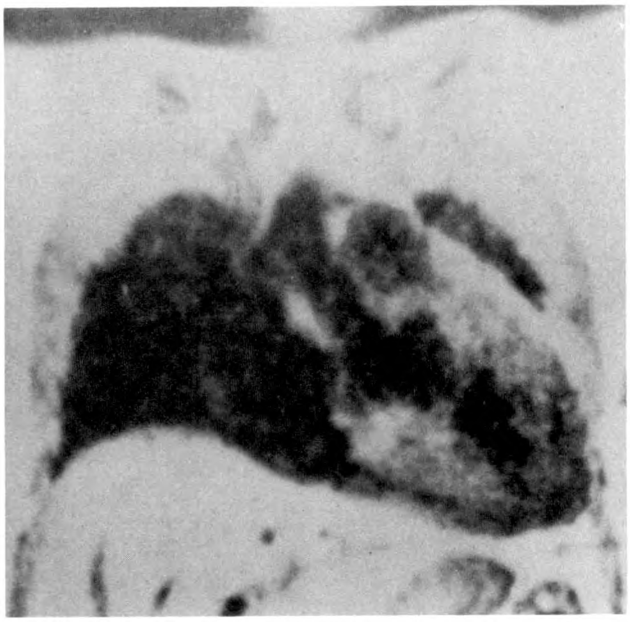

Fig 2. Nuclear magnetic resonance image showing sinus of Valsalva aneurysm protruding into the interventricular septum.

tablish the diagnosis and demonstrate the filling of the sac from the aorta and its pulsation.

Although medical treatment is acknowledged as being adequate for managing cases with intact aneurysm, the poor prognosis associated with rupture mandates early surgical intervention [3, 4]. In our case, operation was deemed necessary and provided clinical improvement. Operation also has prophylactic value in preventing further complications, eg, aneurysmal rupture, intractable heart failure, and progressive aortic regurgitation. Resection of the pouch is unwarranted and can lead to damage to adjoining structures such as the aortic valve or the interventricular septum. Closure of the mouth of the

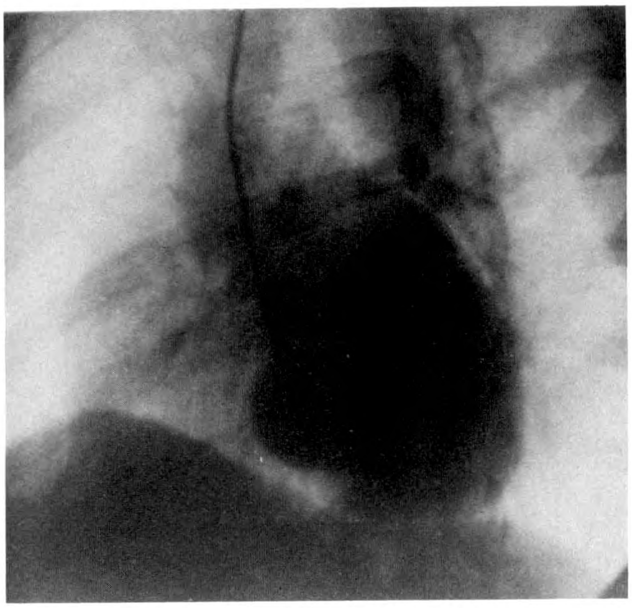

Fig 3. Aortic root angiography (left anterior oblique view) demonstrating large aneurysmal pouch bulging into the interventricular septum.

pouch with autologous pericardium effectively deals with the problem and has the virtue of simplicity.

References

1. Meyer J, Wakasch DC, Hallman GL, Cooley DA. Aneurysm and fistula of the sinus of Valsalva. Ann Thorac Surg 1975;19:170–9.
2. Engel PJ, Held JS, Van der Bel-Kahn, et al. Echocardiographic diagnosis of the congenital sinus of Valsalva aneurysms with dissection of the interventricular septum. Circulation 1981;63:705–11.
3. Jansen EWL, Nauta ILD, Lacquet LK. Ruptured aneurysms of the sinus of Valsalva. Thorac Cardiovasc Surg 1984;32:148–51.
4. Pan-Chin, Chin-Heng T, Chen-Chu, Chieh-Fu L. Surgical treatment of the ruptured aneurysm of the aortic sinuses. Ann Thorac Surg 1981;32:162–6.
5. De Bakey ME, Diethrich EB, Liddicoat JE, Kinard SA, Garrett HE. Abnormalities of the sinuses of Valsalva: experience with 35 patients. J Thorac Cardiovasc Surg 1967;54:312–32.
6. Metras D, Coulibay AO, Ouattara K. Calcified unruptured aneurysm of sinus of Valsalva with complete heart block and aortic regurgitation. Br Heart J 1982;48:507–9.

REVIEW OF RECENT BOOKS

The Aortic Valve

By Mano Thubrikar
Chicago, CRC Press, 1989
240 pp, illustrated, $97.50

Reviewed by Steven F. Bolling, MD

The Aortic Valve by Mano Thubrikar is very interesting in the amount of detail and attention it pays to the aortic valve. Dr Thubrikar is the Director of Surgical Research at the University of Virginia. and his background is in engineering and biomedical engineering. This fact is reflected throughout the book, and one of the failings of this book is its lack of relevance for cardiothoracic surgeons and especially for residents in cardiothoracic surgery. This book spends an inordinate amount of detail and time on geometry, dynamics, mechanical properties, and other engineering concerns regarding the aortic valve. Even the chapters that are not directly related to this kind of engineering concern relate diseases of the aortic valve and echocardiography of the aortic valve to mathematics. I would therefore say that this detailed analysis of the aortic valve is both the strong point and the failing of this book. I think that this book would be useful to thoracic surgeons who were extremely interested in the aortic valve and would be especially helpful to those doing work in homograft aortic root replacement. However, I think it would be of lesser value to thoracic surgery residents beginning their introduction to cardiac surgery.

The book is well written and easily understood. Even the most detailed engineering concepts and principles are easily understood by nonengineers. In that sense I enjoyed the book. However, overall, I would not rate it an absolute necessity to have in a thoracic surgeon's library.

Ann Arbor, Michigan

Primary Cardiac Leiomyosarcomas

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Two patients with primary cardiac leiomyosarcoma, one of the rarest malignant tumors of the heart, are described. The first patient had a tumor of the pulmonary trunk and was admitted with symptoms suggestive of pulmonary thromboembolism. The second had a tumor of the left atrium and had signs and symptoms of mitral valve obstruction and regurgitation. The 2 patients were operated on and later underwent adjuvant chemotherapy. Both died more than 22 months after operation, having required multiple hospital admissions for treatment of complications related to the pathology or the treatment of the primary cardiac leiomyosarcoma. Nonetheless, aggressive surgical excision followed by chemotherapy appears to have improved survival in these patients with primary cardiac leiomyosarcoma, as they are among the longest survivors reported.

(Ann Thorac Surg 1991;51:999–1001)

Primary malignant cardiac tumors are extremely uncommon, and the leiomyosarcomas are among the rarest ones. Only one of these tumors was seen by McAllister [1] in 444 tumors of the heart and pericardium, of which 28% were malignant, and in a review of the literature in 1986, Segesser and co-workers [2] found only 15 cases of primary leiomyosarcoma of the heart. They are highly aggressive, and mean survival, without treatment, is 6 months from the time of diagnosis [3]. Furthermore, the patient described by Segesser and co-workers was allegedly only the third survivor after surgical resection.

We report on two cardiac tumors operated on recently by Dr Antunes and discuss the strategies followed in the treatment of these tumors.

Case Reports

Patient 1

A 33-year-old woman was admitted in July 1987 with a 3-week history of anorexia, tiredness, markedly decreased effort tolerance, dyspnea, chest tightness, and night cough and sweats. In addition, she had 5 or 6 episodes of nonpostural fainting. Her past medical history was unremarkable.

During the clinical examination, she was distressed and dyspneic at rest. The jugular venous pressure was raised and the tender, pulsatile liver was enlarged to 2 to 3 cm. The chest was clear on auscultation, but the roentgenogram showed an enlarged right ventricle and pulmonary artery segment. On heart auscultation, the pulmonary component of the second heart sound was increased, and there was a soft systolic tricuspid regurgitation murmur. The electrocardiogram showed a right-axis deviation to 100 degrees and a right ventricular strain pattern.

The two-dimensional echocardiographic examination performed the day after admission showed that both the anatomy of the left side of the heart and the left ventricular function were normal. The right atrium and right ventricle were enlarged, and the pulmonary artery systolic pressure, estimated by Doppler echocardiography, was 59 mm Hg. There was mild tricuspid regurgitation. Despite antifailure therapy, her condition deteriorated and cardiac catheterization was undertaken, during which the following pressures were measured: mean right atrial, 20 mm Hg (large A wave); systolic right ventricular, 70 mm Hg; mean right pulmonary arterial, 10 mm Hg. The angiography showed a large thrombus in the pulmonary trunk with poor branch perfusion. She was subsequently referred for operation.

Immediately after median sternotomy, there was a cardiac arrest and cardiopulmonary bypass was instituted in extremis. After pulmonary arteriotomy, a large mass was seen circumferentially adherent to the arterial wall, extending to the bifurcation; an endarterectomy had to be performed for complete excision. The remaining layers of the pulmonary artery wall appeared inflamed, and we were unable to determine whether this was a clot at an advanced stage of organization or a tumor. The excised mass measured 30 mm in diameter and 45 mm in length. The pulmonary valve was normal. The histological findings of the specimen showed a high-grade leiomyosarcoma in which the tumor reached the excision lines. The pulmonary artery was thought to be the primary site. Esophagogastroscopy and upper gastrointestinal contrast study; abdominal sonar of liver, kidney, pelvis, and retroperitoneal space; and echocardiography failed to demonstrate any other possible source of the leiomyosarcoma.

Eleven days after the initial operation, the patient was subjected to reoperation aimed at achieving a wider excision of the tumor. The whole main pulmonary artery was removed, including the sinuses, but the valve was

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preserved. The resection was extended to include the bifurcation, of which only the posterior wall was left. The continuity of the pulmonary artery was reestablished by direct suture of the proximal and distal margins posteriorly and augmented by a large bovine pericardial patch anteriorly. A histological examination confirmed leiomyosarcoma arising from the pulmonary trunk; it appeared that the tumor had been completely excised.

The patient was discharged on day 7 after an uneventful postoperative period. Adjunctive chemotherapy or radiotherapy was thought to be of little value and, therefore, was not used immediately. She remained well but was readmitted 5 months later with sudden onset of left-sided pleuritic chest pain aggravated by cough and rigors. A chest roentgenogram showed a very large mass with smooth edges originating from the left hilum. A fine-needle aspiration recovered numerous cells consistent with the diagnosis of sarcoma. Chemotherapy with 70 mg/m^2 of Adriamycin (doxorubicin hydrochloride) and 300 mg/m^2 of dacarbazine was begun and was repeated weekly. After 6 months, this therapeutic regimen was changed to Iphosphamide (3 g monthly). Subsequently, etoposide (1 g) and carboplatin (540 mg) were also given. There was a dramatic reduction of the size of the mass, which almost disappeared from the roentgenogram. She was readmitted on another four occasions for treatment of relatively mild side effects of the chemotherapy, but she died of a massive episode of hemoptysis 22 months after the initial diagnosis.

Patient 2

A 53-year-old female patient was transferred from a peripheral hospital with the diagnosis of acute pulmonary edema. Previously, she had had two similar episodes. She complained of intense fatigue, dyspnea on exertion, and nonproductive night cough.

On examination, she was dyspneic at rest and had a 2-cm nontender liver. On auscultation, there were some crepitations of both lungs. There was a systolic murmur of mitral regurgitation. The chest roentgenogram showed a mild cardiac enlargement and an interstitial edema of the pulmonary bases without vascular redistribution. The electrocardiogram was normal with a sinus rhythm of 100 beats/min, and two-dimensional Doppler echocardiography showed normal left atrium and left ventricle with good function. The mitral valve was thickened and had diminished opening motion.

She improved on antifailure therapy and was discharged with the diagnosis of hypertension and mild mitral disease, only to be admitted 8 days later with a similar episode, which was promptly reversed with medical treatment. A second two-dimensional echocardiography confirmed the diagnosis of mitral valve disease. The valve orifice area was 1.8 cm^2, and there was moderate regurgitation. The pulmonary flow curve showed moderate pulmonary hypertension. During cardiac catheterization, a systolic right ventricular pressure of 45 mm Hg and a pulmonary capillary wedge pressure of 25 mm Hg were measured. Left ventricular angiography demonstrated normal ventricular function and moderate mitral regurgitation. Although the grade of the mitral lesion in the patient did not correlate well with the severity of the symptoms, we decided to operate on her.

During the procedure, performed under standard cardiopulmonary bypass and cardioplegic arrest, a neoplastic formation described as myxomatous, involving the whole of the posterior left atrial wall, was found. The mass extended to the atrial appendage and left pulmonary veins and invaded the mitral valve annulus but not the leaflets, which were normal. However, the tumor caused a degree of obstruction to blood flow into the left ventricle. There were areas of necrosis within the mass. As much tumor as possible was removed from the cavity, but no attempt was made to excise the involved atrial wall because of the extension of the invasion. The histological diagnosis was leiomyosarcoma with myxoid areas.

The patient had an uneventful postoperative recovery and was discharged on the 11th day. She was referred to chemotherapy with a monthly regimen of Metoxantrone (20 mg), dacarbazine (100 mg), and cyclophosphamide (1,000 mg) for 5 months. She was asymptomatic for 6 months and was then admitted with ascitis and hepatomegaly, which responded promptly to antifailure therapy. She had two further admissions for the same reason. On the last occasion, she also had a large right-sided pleural effusion, which recurred after drainage, and a chemical pleurodesis with tetracycline was performed. Two-dimensional Doppler echocardiography showed recurrence of the tumor in the left atrial cavity, and septal and tricuspid valve invasion with moderate regurgitation. No further operation was planned, and the patient refused additional chemotherapy. She died nearly 23 months after operation, probably of a cerebral metastasis.

Comment

Primary leiomyosarcomas of the heart are extremely rare and constitute less than 0.25% of all cardiac tumors [1]. Having in mind that the autopsy incidence of all primary cardiac neoplasms is about 0.002% [4] and that most cases are only diagnosed postmortem, finding of such a tumor is usually a once-in-a-lifetime experience for any one surgeon. In his series of 125 cases of malignant cardiac tumors, McAllister [1] found only one leiomyosarcoma. There was also only 1 case among the 133 surgically treated patients recently reported from the Texas Heart Institute by Murphy and associates [5]. Other large surgical series from the University of Alabama [6] and from Stanford University [7] did not include any case of this histological type. Finally, in their review of the literature, Segesser and colleagues [2] were able to find only one report of 2 cases, of which 1 was operated on. We were able to locate only 9 previously reported cases of surgically treated primary cardiac leiomyosarcomas, including 4 of the pulmonary artery.

Our 2 patients were admitted with symptoms of obstruction: one, of the pulmonary artery, mimicking pulmonary thromboembolism; and the other, of the left atrium, mimicking mitral stenosis with regurgitation. In both patients, the diagnosis was presumptive intraoperatively and was confirmed by histological examination. As wide an excision as possible should be performed, but this could only be achieved at a second operation in the first patient. Although controversial, reoperation may have contributed to prolong the patient's life. In the other patient, debulking of the tumor was the only possibility, as involvement of the pulmonary veins precluded radical excision of the posterior left atrial wall.

The mean survival after diagnosis is 6 months (9 months in patients who had operation), and only one survival longer than 2 years has been reported [8]. These tumors are highly aggressive and locally invasive; therefore, resection is essentially palliative and aims at relieving symptoms of obstruction of valves or major blood vessels. Even in the case of apparent complete removal, the long-term prognosis is poor because of the early local recurrence and appearance of metastases. Both chemotherapy and radiotherapy appear to be only as effective (or as ineffective) as they are for similar tumors of other origins and, generally, for the treatment of sarcomas [9]. Retrospectively, immediate postoperative chemotherapy could have favorably altered the progress of the disease in our first patient, judging by the dramatic effect it had when it was used later.

The hopeless prognosis of primary cardiac leiomyosarcomas has again been demonstrated in our patients, in whom the side effects of adjuvant therapy led to repeated admissions to the hospital. Nonetheless, these 2 patients appear to be among the longest survivors reported. The limited experience of any center in the treatment of these neoplasms makes it difficult to evaluate the relative importance of the two modalities, surgical excision and adjuvant therapy. However, extensive resection and cardiac reconstruction, if required, followed by chemotherapy may considerably prolong patients' lives, as appeared to have happened in our patients.

References

1. McAllister HA Jr. Cardiovascular pathology. New York: Churchill Livingstone, 1983.
2. von Segesser L, Cox J, Gross J, et al. Surgery in primary leiomyosarcoma of the heart. Thorac Cardiovasc Surg 1986;34:391–4.
3. Poule GV, Meredith JW, Breyer RH, Mills SA. Surgical implications of malignant cardiac disease. Ann Thorac Surg 1983;36:484–91.
4. Strauss R, Merliss R. Primary tumor of the heart. Arch Pathol 1945;39:74–8.
5. Murphy MC, Sweeney MS, Putnam JB Jr, et al. Surgical treatment of cardiac tumors: a 25-year experience. Ann Thorac Surg 1990;49:612–8.
6. Kirklin JW, Barrat-Boyes B. Cardiac surgery. New York: John Wiley and Sons, 1986:1393–407.
7. Dein JR, Frist WH, Stinson EB, et al. Primary cardiac neoplasms. Early and late results of surgical treatment in 42 patients. J Thorac Cardiovasc Surg 1987;93:502–11.
8. Eisenmann B, Baherel B, Bareiss P, Jeanblanc B, Warter J, Kieny R. Les sarcomes primitifs de l'artere pulmonaire. Ann Chir Thorac Cardiovasc 1977;16:315–22.
9. Chitwood WR. Cardiac neoplasms. Current diagnosis, pathology, and therapy. J Cardiac Surg 1988;3:119–54.

Long-Term Follow-up of the Vineberg Internal Mammary Artery Implant Procedure

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This report describes the 20-year follow-up of a patient who had undergone a double internal mammary implantation for coronary occlusive disease. A lack of similar reports in the literature suggests that such survival is rare, but this case indeed documents the fact that the internal mammary arteries can revascularize the myocardium, and this patient's continued survival appears to depend entirely on this collateral blood flow.

(Ann Thorac Surg 1991;51:1002–3)

The true long-term success rate of the Vineberg procedure is unclear, but in the year after Dr Vineberg's death, it would seem timely to report on at least 1 patient who owes his continuing existence to internal mammary artery implants.

A 53-year-old man underwent a double internal mammary implantation on April 28, 1969, for occlusive disease of the circumflex, anterior, and posterior descending coronary arteries. The left internal mammary artery was tunneled along the lateral aspect of the left ventricular wall beneath the obtuse marginal branches, and the right was implanted on the inferior surface of the left ventricle.

Coronary angiography was again performed on August 15, 1989. The right coronary, circumflex, and anterior descending arteries were totally occluded. His only native circulation came from two small diagonal branches of the left coronary artery, and there was faint visualization of a small obtuse marginal and a posterior ventricular coronary artery branches. Injection of the internal mammary arteries with contrast medium showed that they were both patent. The left internal mammary artery completely filled the distal anterior descending artery and septal branches and the distal posterior descending artery. An extensive arteriolar blush was seen (Fig 1). The right internal mammary artery injection showed that this vessel was patent, and the terminal distribution on the inferior surface of the heart showed a blush and connection with some small coronary artery branches (Fig 2). Injection of each artery showed the contrast medium filling the coronary sinus. No further surgical intervention appeared possible or even indicated. The patient continues to be maintained on a medical program and functions well.

Comment

It is not the purpose of this study to give a detailed report of the Vineberg operation. On the other hand, a review of the literature has failed to identify reports of long-term follow-up after this procedure. Bhayana and colleagues [1] reported a follow-up extending to 12 years with 58% of the patients dead at 10 years. The patency of single grafts was 50% and double grafts, 68.8% at 1 year. They did not identify improved survival, nor did they identify a correlation between the relief of angina and implant patency. Bigelow and associates [2] reported a 1- to 13-year follow-up. Eighty-three percent of patients showed improvement and an improved work test with 1 patient still alive at 13 years in whom ventricular fibrillation resulted from a contrast medium injection into his implant.

Bigelow and associates, along with Björk and colleagues [3], concluded that graft patency was better when the operation was performed in the presence of anterior descending coronary artery obstruction. Urschel and associates [4] reported a follow-up of 44 patients at 2½ to 5 years, with 20 patients experiencing good results. Ochsner and co-workers [5] correlated the patency of the

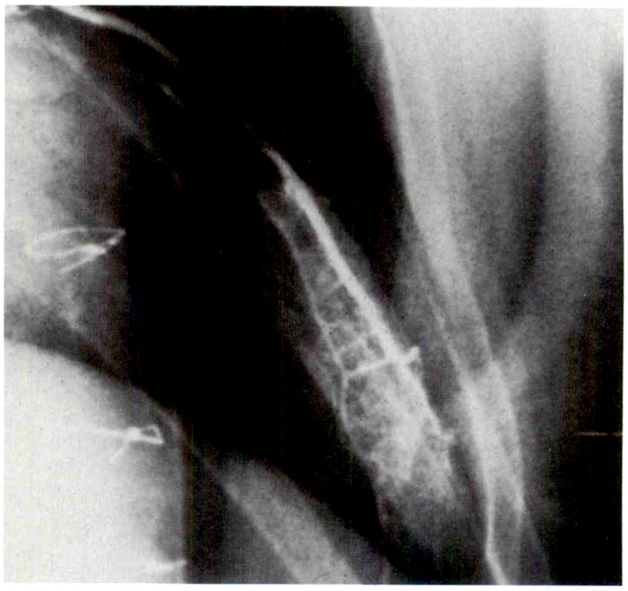

Fig 1. More extensive blush of the myocardium adjacent to the left internal mammary artery implant and the anterior descending coronary artery and some distal filling into the posterior descending artery.

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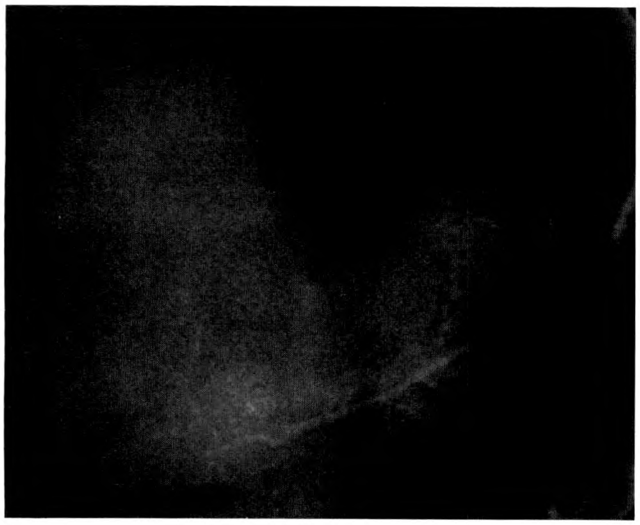

Fig 2. The right internal mammary artery implant showing a blush and arterial filling on the inferior surface of the heart.

implants with the degree of coronary disease and reported a 77% patency of grafts at 6 years. In the presence of severe coronary disease, 95% of the patients had a blush or filling of vessels from the implant. They also reported terminal fibrillation at the time of operation when a patient's implant was divided.

Conclusion

This report describes a greater than 20-year survival of a patient who had undergone a double internal mammary artery implant operation. At this time all major main coronary artery branches are occluded. The lack of other reports in the current literature might indicate that prolonged survival is extremely rare. Although the internal mammary artery implant no longer has a place in the cardiac surgeon's armamentarium, this report and others do perhaps vindicate Vineberg's hypothesis that myocardial internal mammary artery implants can collateralize the circulation of the myocardium. Coronary bypass vein grafts are immediately effective but have limited durability. This report attests to the durability of the internal mammary artery as a graft for bypass or implantation in coronary disease.

References

1. Bhayana JN, Gage AA, Takaro T. Long-term results of internal mammary implantation for coronary artery disease: a controlled trial. Ann Thorac Surg 1980;29:234–42.
2. Bigelow WG, Aldridge HE, MacGregor DC. Internal mammary implantation (Vineberg operation) for coronary heart disease. Ann Surg 1966;164:457–64.
3. Björk L, Cullhed I, Hallen A, Strom G. Result of internal mammary artery implantation in patients with angina pectoris. Scand J Thorac Cardiovasc Surg 1968;2:1–9.
4. Urschel HC, Razzuk MA, Miller ER, Nathan MJ, Ginsberg RJ, Paulson DL. Direct and indirect myocardial revascularization: followup and appraisal. Surgery 1970;68:1087–100.
5. Ochsner JL, Moseley PW, Mills NL, Bower PJ. Long-term followup of internal mammary myocardial implantation. Ann Thorac Surg 1977;23:110–21.

Orthotopic Cardiac Transplantation in Two Patients With Previous Malignancy

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This report presents 2 patients with previous malignancy in whom congestive cardiomyopathy developed secondary to doxorubicin toxicity. Both patients underwent orthotopic cardiac transplantation 3 and 5 years ago and are now in functional class I with no evidence of malignant recurrence.

(Ann Thorac Surg 1991;51:1004–6)

Cancer occurs in transplant recipients with an overall frequency four times that of the age-matched general population. In patients treated with aziothioprine and steroids, 14% of those who survive for 15 years after the transplantation will have cancer other than skin cancer and 44% will have malignant lesions of the skin; with nonskin malignancies, 40% have an association, perhaps casual, with viral infections. Patients with malignancy treated before transplantation are at increased risk for the development of malignancy after transplantation.

Doxorubicin (Adriamycin; Adria Laboratories, Dublin, OH) is one of the most potent chemotherapeutic anticancer agents for adult and childhood solid tumors as well as lymphoma and leukemia. The use of this drug is restricted by its cardiotoxicity, which develops insidiously, causing a congestive cardiomyopathy. Free radical generation and perioxidation of subcellular membranes may be involved. The incidence of myocardiopathy occurs only 0.4% to 1.2%. This report presents 2 patients with sarcomas that were treated aggressively with chemotherapy. Irreversible congestive cardiomyopathy developed, and they were referred for cardiac transplantation. Our first patient had uterine leiomyosarcoma and was 7 months postoperative with no evidence of disease. Our second patient had undergone a leg amputation for osteogenic sarcoma. She had also underwent two lung resections for metastatic disease. At the time of transplantation, she had no evidence of recurrent disease. Both patients are now in functional class I 3 years and 5 years after transplantation and have no evidence of recurrent tumor.

Case Reports

Patient 1

A 38-year-old woman with a history of spontaneous abortions in March and August of 1984 underwent an operation for removal of uterine fibroids in November 1984. Final uterine pathology revealed leiomyosarcoma. She was returned to the operating room for hysterectomy, lymphadenectomy, and peritoneal washing the following day. Although her lymph nodes were negative, the cytology of the wash was positive. Subsequently, the patient received eight doses of doxorubicin for a total of 480 mg/m^2 over 6 months. A planned ninth dose was held because of decreased contractility identified on echocardiogram. Three weeks after her last dose she had increasing symptoms of dyspnea on exertion and orthopnea. A multigated acquisition scan showed a decrease in ejection fraction from 0.42 to 0.19 over this 4- to 6-week period. A cardiac biopsy at that time showed an extensive myofibrillar loss and vacuolization (doxorubicin score of 3) (Fig 1). Her condition deteriorated rapidly despite an intraaortic balloon pump, and she underwent orthotopic cardiac transplantation in June 1985. Despite three bouts of asymptomatic mild rejection in the first 6 months after transplantation she has done well. Now, more than 5 years after transplantation, she is in functional class I and active in her community. She has no evidence of recurrent tumor.

Patient 2

A 22-year-old woman had a right lower leg mass. Incisional biopsy showed osteosarcoma. She subsequently underwent a right above-knee amputation on November 11, 1977. Four months later she underwent a wedge excision of a right lower lobe metastasis. A month later wedge excision of a left lower lobe mass revealed metastatic sarcoma. She was randomized to receive doxorubicin and cyclophosphamide (Cytoxan; Bristol-Myers, Evansville, IN). She received a total doxorubicin dose of 497 mg/m^2 and a cyclophosphamide dose of 1,200 mg/m^2 over 1 year. An echocardiogram in March 1979 revealed decreased left ventricular function and left ventricular enlargement. She received one additional dose of doxorubicin for a total of 540 mg/m^2. She had an uneventful pregnancy with no cardiac symptomology and delivered a child in July 1984. Eight months postpartum progressive congestive heart failure developed and she was hospitalized in April 1985. She did well on medical treatment until April 1987. A multigated acquisition scan at that time

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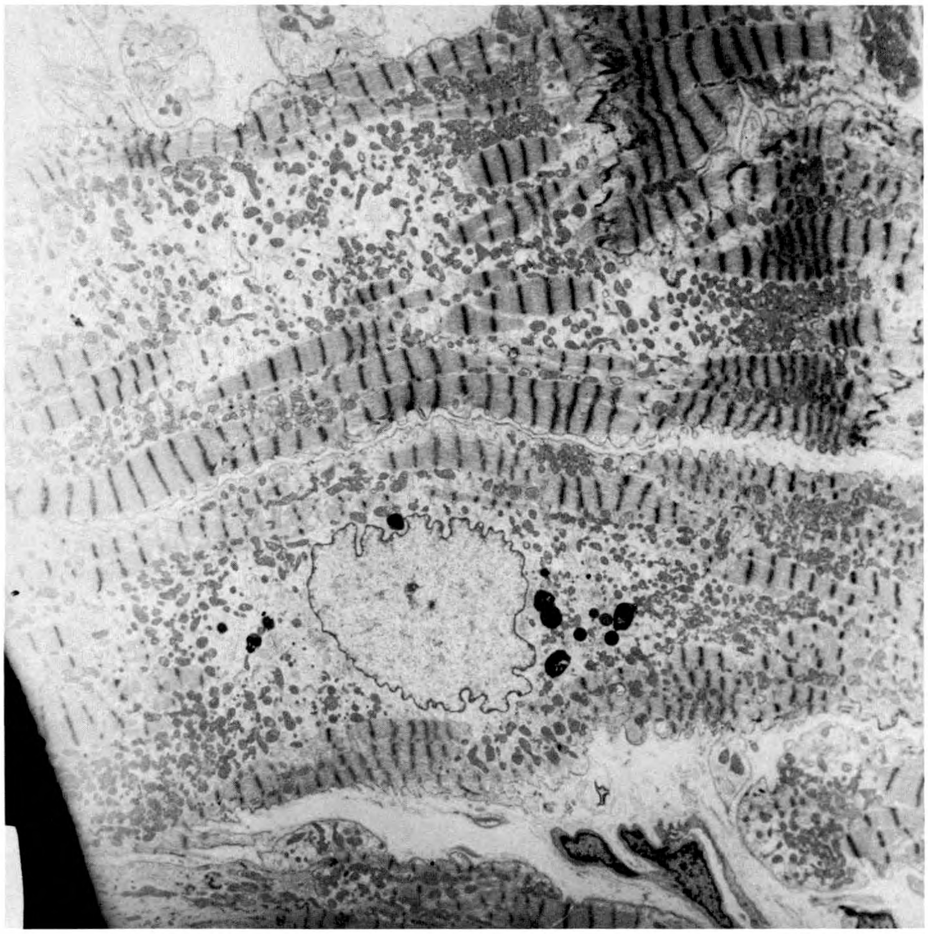

Fig 1. Electron photomicrograph of a myocyte showing almost total loss of contractile elements with only Z bands remaining around the periphery of the cell. (En bloc stain with uranyoacetate; counterstained with lead citrate; × 4,000 before 35% reduction.)

revealed an ejection fraction of 0.14. A cardiac biopsy at that time revealed an doxorubicin toxicity score of 2.5. Progressive class IV heart failure developed, necessitating inotropic support. She underwent an orthotopic cardiac transplantation on June 8, 1987, within 1 week of being listed. At the time of cardiac transplantation she had gone 7 years with no evidence of recurrent disease. Postoperatively, she had one episode of acute rejection at 1 month, which was treated successfully. Her coronary angiogram at 2 years was normal. A multigated acquisition scan demonstrated a right ventricular ejection fraction of 0.52 and a left ventricular ejection fraction of 0.61.

Comment

Cardiac toxicity is the major factor limiting doxorubicin treatment. A single rapid infusion of 60 to 75 mg/m^2 is usually given at 21-day intervals. Doxorubicin binds to tissue (including heart) DNA and inhibits nucleic acid synthesis. There is myocardial interstitial fibrosis with cellular loss. Electron microscopy shows loss of contractile substance and swelling of mitochondria and T-tubules [1, 2]. The histopathological lesions of doxorubicin toxicity are focal but disseminated throughout the heart.

The cardiotoxic effects may be acute, subacute, or chronic. A toxic myocarditis and occasionally pericarditis may occur within days or weeks, often related to a single high dose. When it occurs, rapidly progressive biventricular failure usually appears 1 to 6 months after completion of chemotherapy.

It is now well known that the cardiotoxic effects of doxorubicin are dose related and that the evidence climbs rapidly in patients receiving a total dose greater than 550 mg/m^2. Previous mediastinal irradiation, cyclophosphamide, age greater than 70 years, and preexisting heart disease also increase the likelihood of cardiotoxicity at lower doses [3].

Billingham and associates [4] have found that grading the actual histopathological lesions is an accurate method for estimating the degree of cardiac injury and, therefore, the patient's ability to tolerate additional dosages. The classification of cardiac toxicity on biopsy is as follows: grade 0, no change from normal myocardium; grade 1, sparsely affected myocytes (myofibrillar loss or sarcotubular vacuolization) (continue doxorubicin administration); grade 2, groups of affected myocytes with myofibrillar loss or sarcotubular vacuolization (continue doxorubicin administration); grade 3, extensive myocyte change of myofibrillar loss or vacuolization (no more doxorubicin should be given). Bristow and co-workers [5, 6] used this grading in conjunction with right heart catheterization data to develop a similar toxicity scale. Histological grading confirmed evidence of doxorubicin-related cardiac damage in both of our patients' hearts before transplantation.

Our first patient received slightly less than 500 mg/m^2 of doxorubicin. Patients receiving this dose usually represent only 1% to 2% of all patients with cardiac toxicity. A cardiac biopsy grade of 3, however, clearly identified anthracycline toxicity. One month after her diagnosis of cardiac toxicity she decompensated, requiring mechanical ventilation, an intraaortic balloon pump, and intravenous inotropic support with dobutamine and amrinone (Inocor; Winthrop Pharmaceuticals, New York, NY). Cardiac transplantation was considered despite leiomyosarcoma recurrence rates as high as 50% because of her young age, moderate mitotic activity (8 to 9 per 10 high-power fields), and only minimal cytology with no evidence of lymph node or pelvic involvement. Her pretransplantation work-up revealed no evidence of recurrent sarcoma. A chest roentgenogram and computed tomographic scale were negative.

Severe congestive heart failure developed in our second patient almost 6 years after her last dose of doxorubicin. Her doxorubicin regimen was discontinued in February 1979 because of marked decreased cardiac function on echocardiogram. Her congestive heart failure began in April 1985. At that time, because there was no further progression, her osteosarcoma was believed to be cured. A cardiac biopsy was performed before cardiac transplantation. Her biopsy score of 2.5 clearly identified doxorubicin toxicity. She received cyclophosphamide, which is known to be synergistic with doxorubicin and probably contributed to her cardiomyopathy. The decision for cardiac transplantation in this patient was easier because at 7 years, with no recurrent tumor, she was essentially cured.

Malignancy is an obvious relative contraindication to transplantation. Patients with a history of cancer before transplantation are twice as likely to have development of cancer after transplantation. In general, fewer recurrences occur with greater time from treatment of cancer. Penn [7], reviewing 119 patients with epithelial tumors involving a wide variety of internal organs who went on to organ transplantation, showed there were 17 (40%) in whom recurrences or metastases developed, mostly from the tumors of the breast, bladder, and colorectum. In general, the greater the time from treatment of cancer to transplantation, the fewer recurrences occurred. However, 5 (29%) of the 17 recurrences occurred in patients who had been treated an average of 7 years before transplantation. Most clinicians usually favor transplantation after cancer when the time from treatment to transplantation is 1 or preferably 2 years. The recurrence rate decreases markedly at 2 years.

Both patients underwent extensive work-up including chest roentgenography, computed tomographic scans, bone scans, and bone marrow aspiration to exclude either metastic or recurrent sarcoma. Our first patient was seen only 6 months after treatment but was considered because of complete surgical removal and only mildly positive cytology. Our second patient, seen at 7 years, clearly had been cured. In both patients aggressive chemotherapy for sarcoma resulted in therapeutic cures but serious end-organ damage. In this subset of patients we believe cardiac transplantation ought to be considered. Both women are currently in functional class I and in remission 3 and 5 years after orthotopic cardiac transplantation.

We give special thanks to Margaret Billingham, Department of Pathology, Stanford University, Stanford, California, for electron photomicrographs.

References

1. Lefrak EA, Hia P, Rosenheim S, Gottlieb JA. A clinicopathologic analysis of Adriamycin cardiotoxicity. Cancer 1973; 32:302–14.
2. Buja LM, Ferrans VJ, Mayer RJ, Roberts WC, Henderson ES. Cardiac ultrastructural changes induced by daunrubicin therapy. Cancer 1973;32:771–88.
3. Minow RA, Benjamine RS, Lee ET, Gottliebe JA. Adriamycin cardiomyopathy—risk factors. Cancer 1977;39:1397–402.
4. Billingham ME, Mason JW, Bristow MR, Daniels JR, Anthracycline cardiomyopathy monitored by morphologic changes. Cancer Treat Rep 1978;62:865–72.
5. Mason JW, Bristow ME, Billingham ME, Daniels JR. Invasive and non-invasive methods of assessing Adriamycin cardiotoxicity in man: superiority of histopathologic assessment using endomyocardial biopsy. Cancer Treat Rep 1978;62:857–74.
6. Bristow MR, Mason JW, Billingham ME, Daniels JR. Dose-effect and structure-function relationships in doxorubicin cardiomyopathy. Am Heart J 1981; 102:709–18.
7. Penn J. Renal transplantation in patients with pre-existing malignancies. Transplant Proc 1983;15:1079–82.

Mitral Valve Replacement in Idiopathic Hypereosinophilic Syndrome

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Idiopathic hypereosinophilic syndrome is an eosinophil-mediated tissue injury causing multiple organ failure. Cardiac manifestations include subendocardial fibrosis, thrombus leading to peripheral emboli, restrictive cardiomyopathy, and valvar dysfunction. This article describes a patient with the syndrome and reviews surgical experience with valve replacement and long-term prognosis.

(Ann Thorac Surg 1991;51:1007–9)

Idiopathic hypereosinophilic syndrome (IHS) is an uncommon clinical problem marked by an unexplained, persistent eosinophilia of 1.5 eosinophils × 10^9/L (1,500/μL). Multiple organ system dysfunction secondary to eosinophilic infiltration or eosinophil-mediated tissue injury is characteristic [1–3]. Cardiovascular manifestations of the syndrome are the major source of morbidity and mortality [4] and include progressive subendocardial fibrosis with thrombus formation leading to peripheral emboli, restrictive cardiomyopathy, and valvar dysfunction [1, 4]. This case report illustrates the challenge to the cardiac surgeon that such patients may present, and reviews the current experience with valve replacement and long-term prognosis.

A 38-year-old woman with a 5-month history of mitral insufficiency was admitted to our hospital with acute occlusion of the left femoral artery. On admission, she had a leukocytosis of 43 × 10^9/L (43,000/μL) with 91% eosinophils, and underwent successful femoral embolectomy. The postoperative course was marked by an unexplained eosinophilia, increasing congestive heart failure, and a second embolic event involving the left lower extremity which required another embolectomy. Echocardiography revealed mitral stenosis with mitral regurgitation, vegetations on the mitral valve, and decreased left ventricular cavity size with moderate left atrial enlargement.

Because of cardiac deterioration she underwent an emergent mitral valve replacement with a 25-mm Björk-Shiley prosthesis. Intraoperative findings included thickened, organized fibrinous material in the subvalvar area involving both leaflets of the mitral valve and cavity obliteration of the left ventricle. This pathological material was excised with the native valve before insertion of a low-profile prosthesis. The tricuspid valve was involved to a lesser degree but did not require repair or replacement. The postoperative course was uneventful and the patient was discharged receiving warfarin sodium, hydroxyurea, and prednisone; she had a stable leukocyte count. She remained asymptomatic with this medical regimen, and 4 months later administration of prednisone and hydroxyurea was discontinued. The leukocyte count remained between 10 and 11 × 10^9/L (10,000 to 11,000/μL), and repeat echocardiography showed normal prosthetic valve function.

Seventeen months postoperatively hypotension and pulmonary edema developed. Echocardiography revealed malfunction of the Björk-Shiley prosthesis. The leukocyte count was 19 × 10^9/L (19,400/μL) with 16% eosinophils. Prothrombin time was 29 seconds. Thrombectomy of the mitral prosthesis was performed. Histology of the thrombus showed numerous eosinophils. The postoperative course was complicated by a left hemispheric stroke from which she recovered. She was maintained on warfarin sodium, prednisone, and hydroxyurea.

Subsequent attempts to wean her from steroids resulted in increasing eosinophilia, and 26 months later valve thrombus recurred which required thrombectomy. The tilting disc had normal disc excursion after removal of the pathologic fibrinous material and thrombus. Recovery was uneventful and she was discharged receiving warfarin sodium, prednisone, and hydroxyurea with satisfactory control of her eosinophilia.

Within 1 month thrombotic valve obstruction recurred again. The Björk-Shiley prosthesis was replaced by a 27-mm St. Jude prosthesis. Subendocardial resection of extensive organized thrombus was required before insertion of the new prosthesis. The postoperative course was uneventful. Eosinophilia has remained well controlled by prednisone and hydroxyurea with freedom from subsequent thromboembolic complications 34 months postoperatively.

Comment

There are many disorders associated with secondary eosinophilia, a subject that has been extensively reviewed [5]. However, eosinophilia may be seen in patients without evidence of other disorders known to cause secondary eosinophilia. When associated with multiple organ system dysfunction, the condition is known as the idiopathic

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Table 1. Summary of Surgical Experience in Idiopathic Hypereosinophilia Syndrome[a]

Author	No. of Patients	Operation	Follow-up	Outcome
Bell et al, 1976 [10]	1	Mitral annuloplasty	6 mo (no further F/U)	Alive and well
Weyman et al, 1977 [11]	1	MVR with porcine, TV commissurotomy	6 mo (no further F/U)	Alive and well
Fauci et al, 1982 [1, 12]	1	MVR/TVR with Björk-Shiley	Recurrent thromboemboli, redo MVR, TVR with porcine valves	Died at 8 mo
	1	MVR/TVR with porcine	7 mo (8 y)	Alive and well
	1	MVR with porcine	13 mo (4 y)	Died—bone marrow infection
Fourmid et al, 1982 [13]	1	TVR	4 y (6 y)	Alive and well
Blake et al, 1985 [14]	1	MVR with porcine	11 mo (5 y)	Alive and well
Hendren et al, 1988 [9]	1	AVR/MVR with St. Jude	Acute valve dysfunction requiring repeat AVR/MVR with porcine at 12 mo (no further F/U)	Alive and well

[a] Follow-up information in parentheses was obtained by personal communication with authors.

AVR = aortic valve replacement; F/U = follow-up; MVR = mitral valve replacement; TVR = tricuspid valve replacement.

hypereosinophilic syndrome or Loeffler's syndrome. The extent of systemic involvement is variable but can range from minor skin lesions to serious cardiovascular and neurological dysfunction. The cardiovascular manifestations of this syndrome comprise the major source of morbidity and mortality [4].

The association of hypereosinophilia with cardiac disease dates back to Loeffler's original description in 1936 [6]. The cardiac pathology has been well described [1, 7, 8] and consists primarily of endocardial fibrosis with superimposed mural thrombus. This thrombotic process can lead to restrictive cardiomyopathy and restriction of valve leaflet mobility. Valve involvement most commonly results in atrioventricular regurgitation, although aortic valve involvement has been less critical [9]. Thirty percent of patients in the National Institutes of Health series had clinically significant and progressive mitral regurgitation [1]. Thrombosis of small intramural coronary vessels may occur in addition to eosinophilic infiltration of the endocardium and myocardium [1, 7] causing ventricular dysfunction.

A review of the syndrome by Parillo and associates [3] revealed a mortality of 77% within 3 years, and because of this poor prognosis, an aggressive medical regimen consisting of prednisone and hydroxyurea was initiated. Survival improved with a 3-year mortality of 4% in 26 patients and a 10-year survival of almost 70% in 50 patients [1].

The surgical experience of patients with cardiac involvement secondary to IHS is limited (Table 1). However, our experience mirrors that of others in that mechanical valves have a high incidence of thrombotic problems occurring in the setting of adequate anticoagulation and poor control of eosinophilia. The choice between a mechanical prosthesis and a bioprosthesis for valve replacement in IHS poses a difficult problem for the operating surgeon. Patients with IHS are seen at a young age (20 to 50 years) with small ventricular cavities under less than ideal clinical circumstances. A bioprosthesis should probably be used in all adequately sized ventricles in which no outflow tract obstruction might occur after bioprosthetic placement. Although bioprostheses, which have a lower complication rate in IHS, are preferred, mechanical prostheses should be reserved for patients with left ventricular cavity obliteration. Whenever a mechanical prosthesis is used, regular follow-up for signs of valve dysfunction is necessary, especially during episodes of rising or uncontrolled eosinophilia. We agree with the conclusions of Harley and associates [12] and Hendren and co-workers [9] that to minimize the risk of prosthetic valve thrombosis, the control of peripheral eosinophilia is imperative.

Our patient demonstrated the typical findings of marked eosinophila with a restrictive, thrombotic process involving the mitral valve. She has survived multiple operations for valve dysfunction with follow-up of 79 months since she was first seen. The success of the St. Jude prosthesis compared with the Björk-Shiley is probably due to subsequent excision of fibrotic and thrombotic subvalvar elements, optimal leaflet excursion, and improved control of the peripheral eosinophilia. The patient remains free from further thromboembolic events 30 months after the last operation.

References

1. Fauci AS, Harley JB, Roberts WC, et al. The idiopathic hypereosinophilic syndrome: clinical, pathophysiologic, and therapeutic considerations. Ann Intern Med 1982;97:78–92.
2. Chusid MJ, Dale DC, West BC, Wolff SM. The hypereosinophilic syndrome: analysis of fourteen cases with review of the literature. Medicine 1975;54:1–27.
3. Parrillo JE, Fauci AS, Wolff SM. The therapy of hypereosinophilia syndrome. Ann Intern Med 1978;89:167–72.
4. Parrillo JE, Borer JS, Henry WL, et al. The cardiovascular

manifestations of the hypereosinophilic syndrome. Am J Med 1979;67:572–82.
5. Ottesen EA, Cohen SG. The eosinophil, eosinophilic, and eosinophil related disorders. In: Middleton JRE, Reed CE, Ellis EF, eds. Allergy: principles and practice. St. Louis: C.V. Mosby, 1978:584.
6. Loeffler W. Endocarditis parietelis fibroplastica mit Bluteosinophilic. Ein eigenartiges Krankheitzbild. Scheiz Med Wochenschr 1936;66:817–20.
7. Somers K, Hutt MSR, Patel AK, et al. Endocardial biopsy in diagnosis of cardiomyopathesis. Br Heart J 1971;33:822–32.
8. Olsen EGJ, Path FRC, Spry CJF. The pathogenesis of Loeffler's endomyocardial disease and its relationship to endomyocardial fibrosis. Prog Cardiol 1979;8:281–303.
9. Hendren WE, Jones EJ, Smith MD. Aortic and mitral valve replacement in idiopathic hypereosinophilic syndrome. Ann Thorac Surg 1988;46:570–1.
10. Bell JA, Jenkins BS, Webbe-Peploe MM. Clinical, hemodynamic, and angiographic findings in Loeffler's eosinophilic endocarditis. Br Heart J 1976;38:541–8.
11. Weyman AE, Rankin R, King H. Loeffler's endocarditis presenting as mitral and tricuspid stenosis. Am J Cardiol 1977;40:438–44.
12. Harley JB, McIntosh CL, Kirklin J. Atrioventricular valve replacement in the idiopathic hypereosinophilic syndrome. Am J Med 1982;73:77–81.
13. Fourmid G, Schlanger R, Berthoumien F, et al. Surgery for cardiac complications caused by endocardial mural fibrin deposits in hypereosinophilic syndrome. Circulation 1982;65:1010–4.
14. Blake DP, Palmer TE, Olinger GN. Mitral valve replacement in idiopathic hypereosinophilic syndrome. J Thorac Cardiovasc Surg 1985;89:630–8.

The European Association for Cardio-Thoracic Surgery Notice of Annual Meeting

The Fifth Annual Meeting of the European Association for Cardio-Thoracic Surgery will be held September 22–25, 1991, at the Royal Lancaster Hotel in London, United Kingdom. The scientific sessions are open to all registered participants. The registration fee includes admission to the entire scientific program, meeting documentation, welcome reception on Sunday evening, concert on Monday evening, and tea and coffee.

Registration and Hotel Reservation

All participants of the meeting should request a registration form from Conference Associates & Services Ltd, EACTS, Congress House, 55 New Cavendish St, London W1M 7RE, United Kingdom (telephone: 071 486 0531; facsimile: 071 935 7559).

Pneumonectomy Secondary to *Mycobacterium fortuitum* in Infancy

Ralph F. Paone, MD, Leo C. Mercer, MD, and Bertram A. Glass, MD

Department of Surgery, Texas Tech Regional Academic Health Science Center, El Paso, Texas

Severe necrotic lung disease as a result of infection with a rapidly growing mycobacteria occurred in a 4-month-old infant. Successful treatment required a pneumonectomy.

(Ann Thorac Surg 1991;51:1010–1)

The nontuberculous mycobacteria of Runyon's group IV are rapidly growing and include the human pathogens *Mycobacterium fortuitum* and *Mycobacterium chelonei*. These bacteria only rarely cause pulmonary disease in adults. Successful treatment is usually achieved with antibiotic therapy alone. We describe a case of an infant with a necrotizing pneumonia caused by this group of organisms. A brief review of this disorder follows.

A 4-month-old male infant was referred to our institution on May 6, 1989, because of respiratory distress. The child was born in Mexico by spontaneous vaginal delivery without complications. He developed normally until 6 weeks of life, at which time he began having mild respiratory difficulty. A short course of antibiotics was prescribed by a local physician but the child failed to respond. He was then hospitalized in Mexico where he received aminoglycoside and cephalosporin antibiotics for a right upper lobe pneumonia. The infant's condition failed to improve, and after 3 weeks of antibiotics was sent to the Texas Tech Clinics for evaluation.

On physical examination, the child was cachectic and in mild respiratory distress with tachypnea and nasal flaring. His respiratory rate was 50 breaths/min, his heart rate was 175 beats/min, and his temperature was 40°C. Breath sounds were diminished over the right hemithorax. There was no adenopathy present. A chest radiograph (Fig 1) on admission showed consolidation of the right middle and upper lobes. The child was started on a regimen of antibiotics, and a computed tomographic scan of the chest (Fig 2) was obtained. This revealed a large, solid right lung mass with little functioning lung. An anterolateral thoracotomy and open lung biopsy were subsequently performed. Cultures of the tissue grew *M fortuitum*, for which he was started on a regimen of amikacin and Bactrim (trimethoprim and sulfamethoxazole; Roche Laboratories, Nutley, NJ). An assay for human T-cell lymphotropic virus type III had negative results. His condition did not improve, and a follow-up computed tomographic scan at 5 weeks showed no resolution of the lung consolidation. A pulmonary perfusion scan (Fig 3) showed minimal blood flow to the right lung.

A right pneumonectomy was performed after 6 weeks of antibiotic treatment. At operation, the right lung was necrotic except for the medial segment of the middle lobe. Cultures of the lung were positive for *M fortuitum*. Histological examination of the specimen revealed extensive caseating granulomatous inflammation containing acid-fast bacilli (Fig 4). The child recovered well from the operation and was discharged from the hospital 14 days later.

Comment

The nontuberculous mycobacteria of Runyon's group IV are rapidly growing and include the human pathogens *M chelonei* and *M fortuitum* [1]. These organisms have recently been recognized as etiologic factors in human diseases. Hand and Sanford [2] presented one of the earliest reports of infections due to *M fortuitum* in 1970. These cases were mainly soft tissue infections. Subsequently, *M fortuitum* and *M chelonei* were described in association with disseminated disease, cutaneous infections, postoperative infections, and pulmonary disease.

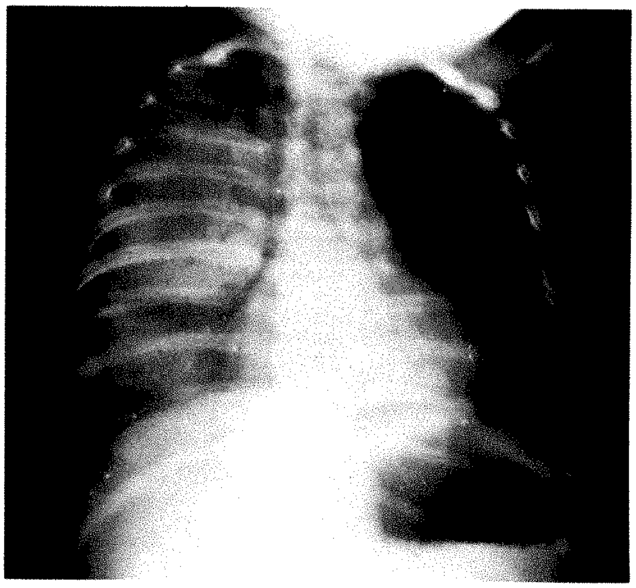

Fig 1. Chest radiograph on admission.

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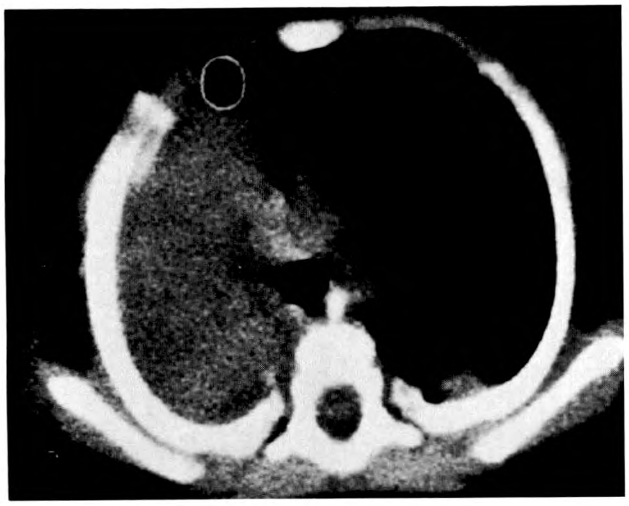

Fig 2. Computed tomographic scan of chest.

There have been few reports of pulmonary disease associated with the rapidly growing mycobacteria. In 1973, Tsukamura and associates [3] described 9 cases of pulmonary disease associated with *M chelonei*. These patients were all adults. Sopko and co-workers [4] presented 4 cases of pulmonary infections caused by these organisms. All patients were adults with underlying emphysema. Bevelaqua and colleagues [5] and Gruft and Henning [6] described cases of pulmonary disease caused by the rapidly growing mycobacteria. These patients were all elderly, debilitated, and with concurrent lung disease. Indeed, most cases of lung disease caused by the rapidly growing mycobacteria have been in adults with preexisting pulmonary pathology.

The 4-month-old patient we describe had failure to thrive, fevers, and respiratory distress. His chest radiograph revealed a pneumonia without cavitation. The computed tomographic scan showed a solid mass initially thought to be a tumor. *Mycobacterium fortuitum* was subsequently cultured from the right lung and reportedly was sensitive to amikacin and Bactrim. The child did not improve with this regimen and required a right pneumonectomy for successful treatment.

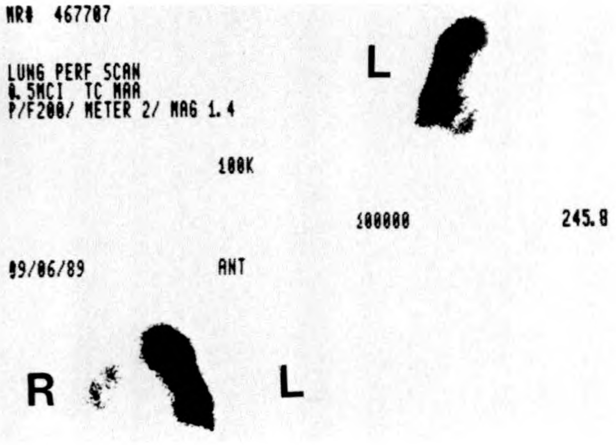

Fig 3. Pulmonary perfusion scan.

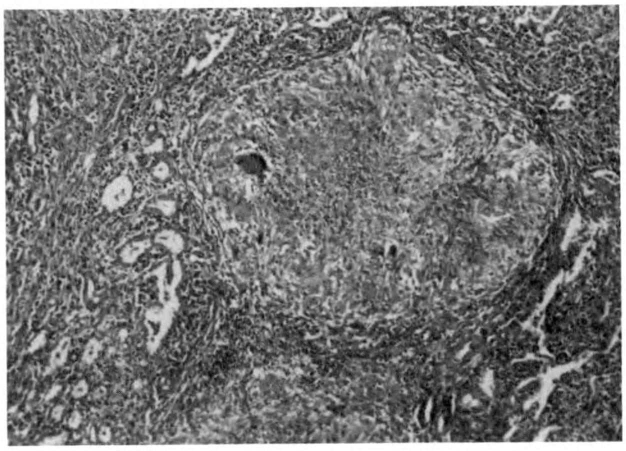

Fig 4. Mycobacterium fortuitum *(Kinyon's stain).*

Adults with pulmonary infections due to the rapidly growing mycobacteria usually respond to antibiotics, obviating the need for operation [7]. In the case presented, the infant was given a 6-week course of appropriate antibiotics with no response. It may be that the virulence of these organisms is greater in children than in adults. Alternatively, this infant's disease may have rendered his lung necrotic at the time when he was first seen.

This case is presented because pulmonary disease associated with the rapidly growing class of nontuberculous mycobacteria appears to be unusual in infants and young children. The organism was resistant to chemotherapy that reportedly is effective in controlling this disease. Finally, the rapid progression to a necrotic lung and subsequent need for a pneumonectomy to treat the disease is of interest.

References

1. Dinksky EW. Nontuberculous mycobacterial infections of man. Med Clin N Am 1974;58:639–45.
2. Hand WL, Sanford JP. *Mycobacterium fortuitum*—a human pathogen. Ann Intern Med 1970;73:971–7.
3. Tsukamura M, Nakanura E, Kurita I, Nakamura T. Isolation of *Mycobacterium chelonei* subspecies chelonei (*Mycobacterium borstelense*) from pulmonary lesions in nine patients. Am Rev Respir Dis 1973;108:683.
4. Sopko J, Fieselmann J, Kasik, J. Pulmonary disease due to *Mycobacterium chelonei* subspecies *abscesses*: a report of four cases. Tubercle 1980;61:165–9.
5. Bevelaqua F, Kamelher D, Campion J, Christianson L. *Mycobacterium fortuitum-chelonei*. NY State J Med 1981;81:1621–4.
6. Gruft M, Henning H. Pulmonary mycobacteriosis due to rapidly growing acid-fast bacillus, *Mycobacterium chelonei*. Am Rev Respir Dis 1972;105:618–20.
7. Woods G, Washington J. Mycobacterium other than *Mycobacterium tuberculosis*: review of microbiologic and clinical aspects. Rev Infect Dis 1987;9:275–90.

Liposarcoma of the Esophagus

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Liposarcoma is one of the most common soft tissue sarcomas found in adults, yet it rarely develops in the alimentary tract. This report describes the pathological features and management of a liposarcoma of the esophagus.

(Ann Thorac Surg 1991;51:1012–3)

Of the soft tissue sarcomas developing in adults, liposarcoma is one of the most common. It is usually found in the thigh or retroperitoneum [1]; less frequent sites are the chest wall, breast, omentum, and mediastinum [1]. In the digestive tract liposarcoma has been described as a primary tumor in the stomach [2], ileum [3], and cervical esophagus [4]. We report a case of a liposarcoma developing in the thoracic esophagus.

A 68-year-old man was referred with a 1-month history of progressive dysphagia. He was dehydrated but otherwise examination and routine blood tests were normal. Barium swallow showed an intraluminal, polypoid mass in the lower third of the esophagus (Fig 1). At esophagoscopy a nonulcerating, polypoid tumor almost completely obstructed the esophagus 33 cm from the incisor teeth. Attempted biopsy of the lesion produced normal squamous mucosa only.

Despite the negative histology, the radiographic appearances were of a tumor and the patient was rehydrated in preparation for resection. At operation, through a left thoracolaparotomy incision, the tumor was found to lie in the distal esophagus. It had penetrated the muscle of the esophageal wall but was not invading adjacent structures and there was no associated lymphadenopathy. Subtotal esphagectomy was performed with a cervical gastroesophageal anastomosis.

The resected specimen consisted of 11 cm of esophagus with a cuff of stomach up to 4.5 cm in length. The distal esophagus contained a polypoid, gelatinous, focally hemorrhagic tumor which was 7 cm in diameter and arose in the esophageal wall. Histological examination showed a myxoid type of liposarcoma composed of lipoblasts set in a myxoid matrix within a plexiform capillary network (Fig 2). Although the tumor had breached the esophageal wall, local excision was complete with no evidence of nodal metastases.

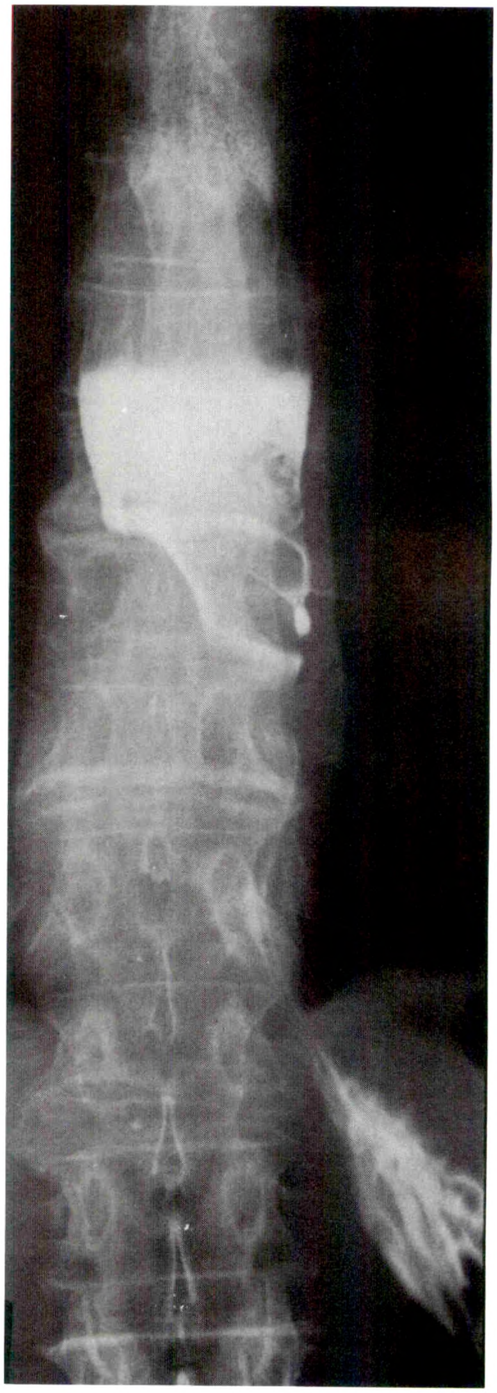

Fig 1. Barium swallow showing the polypoid mass within the esophageal lumen.

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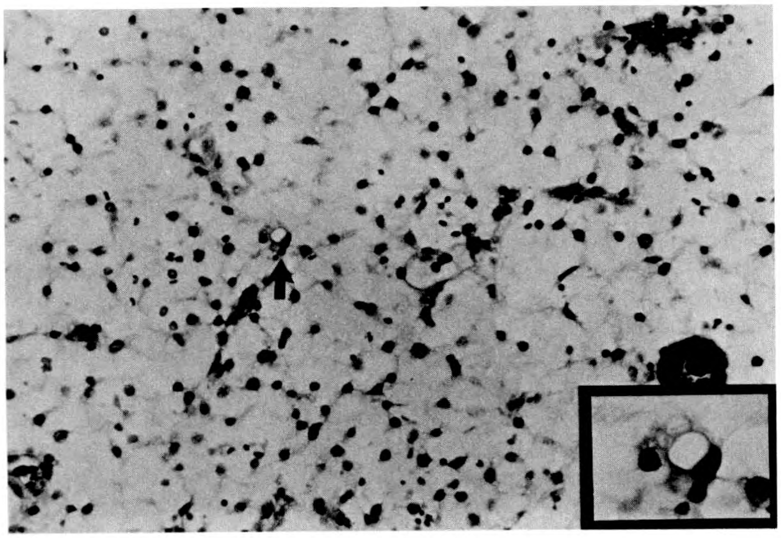

Fig 2. Photomicrograph of esophageal liposarcoma containing typical lipoblasts with vacuolated cytoplasm (arrow *and inset). (Hematoxylin and eosin, ×64 (inset ×160) before 40% reduction.)*

One year later the patient requires occasional dilation of a benign anastomotic stricture but has no evidence of recurrence.

Comment

Several types of sarcoma occur in the esophagus but all are rare [5]. The only type occurring with any frequency is leiomyosarcoma, yet this accounts for only 0.5% of all esophageal malignancies [6]. Liposarcoma of the esophagus has been reported previously; Mansour and associates [4] described a pedunculated liposarcoma arising in the cervical esophagus. In their case the tumor was removed completely by local excision as the pedicle was not involved and the patient had no evidence of recurrence 1 year later.

In the case reported here the tumor, although polypoid, was not pedunculated and arose in the wall of the distal thoracic esophagus. The histological appearances were unequivocally those of a liposarcoma with readily identifiable lipoblasts. There was no clinical evidence of primary or secondary tumor elsewhere. Liposarcoma is believed to originate from primitive mesenchymal cells rather than mature adipose tissue; the presence of normal fat cells is not a prerequisite for its development. Indeed, liposarcomas are rare in subcutaneous fat and the subserosa of the intestinal tract, which are the most common sites of benign lipomas [2]. In this case it is postulated that the tumor took origin from primitive mesenchymal cells of the esophageal wall.

It is not possible to accurately assess prognosis on the basis of 1 case but this patient is alive, without evidence of recurrence, 1 year after resection of a tumor breaching the esophageal wall, suggesting that, in common with liposarcoma elsewhere in the aerodigestive tract [4, 7], surgical excision may offer the best chance of cure.

References

1. Enzinger FM, Weiss SW. Liposarcoma. In: Enzinger FM, Weiss SW, eds. Soft tissue tumours. 2nd ed. St. Louis: C.V. Mosby, 1988:346–82.
2. Shokouh-Amiri MH, Hansen CP, Moesgaard F. Liposarcoma of the stomach. Acta Chir Scand 1986;152:389–91.
3. Chandra RS, Srinivasan V, Bhaskar AG. Liposarcoma of the ileum with secondaries in the liver. Am J Gastroenterol 1972;58:172–6.
4. Mansour KA, Fritz RC, Jacobs DM, Vellios F. Pedunculated liposarcoma of the esophagus: a first case report. J Thorac Cardiovasc Surg 1983;86:447–50.
5. Murray GF. Less common malignant tumours of the esophagus. In: Shields TW, ed. General thoracic surgery. 2nd ed. Philadelphia: Lea & Febiger, 1983:898–911.
6. Rainer WG, Brus R. Leiomyosarcoma of the esophagus: review of the literature and report of three cases. Surgery 1965;58:343–50.
7. Wenig BM, Weiss SW, Gnepp DR. Laryngeal and hypopharyngeal liposarcoma. A clinicopathological study of 10 cases with a comparison to soft-tissue counterparts. Am J Surg Pathol 1990;14:134–41.

Mitral Valve Replacement Six Years After Cardiac Transplantation

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A 33-year-old man found to have increasing mitral regurgitation and decreasing exercise tolerance 6 years after cardiac transplantation received a mitral bioprosthesis. For 8 months he has been without complications from the valve replacement and is clinically and hemodynamically considerably improved.

(Ann Thorac Surg 1991;51:1014–6)

At the University of Arizona, since 1979, we have retransplanted hearts in eight of our 248 heart transplant cases. Given the current shortage of donor hearts, we believe that the decision for retransplantation should not be easy and that other alternatives including conventional procedures should be considered when reasonable. In this report, the case of a chronic cardiac recipient who was treated with mitral valve replacement is documented.

Our patient, a 33-year-old man, had undergone cardiac transplantation for idiopathic cardiomyopathy 6 years previously in 1984. His donor heart, which came from a 42-year-old woman, was believed to be entirely normal, and there was no evidence on echocardiogram of mitral regurgitation. One week postoperatively *Staphylococcus aureus* mediastinitis developed and required drainage, debridement, and closed irrigation followed by prolonged antibiotic therapy. He had one major rejection episode and few other complications until the time of his mitral valve replacement. Table 1 documents yearly follow-up studies as well as his therapy and renal function. Of note, in this table, is some mitral regurgitation from the first year onward. He was hypertensive and had development of concentric left ventricular hypertrophy by the second year. His exercise tolerance test revealed an ischemic response by the fourth year, and his ejection fraction decreased during the fifth and sixth years, corresponding to a slight increase in mitral regurgitation and left- and right-sided filling pressures. Clinically, during the fifth and sixth years, he began complaining of increasing tiredness and shortness of breath. Transesophageal echocardiography 1 week before his mitral valve replacement demonstrated two jets, one central and smaller which hugged the posterior leaflet and a second eccentric dominant jet which appeared to be coming through the posterior leaflet. The patient's functional classification had deteriorated from class I to somewhere between class II and III at the time of his operation.

At operation, on March 27, 1990, there was no gross coronary artery disease. The mitral valve appeared "thinned out." The posterior leaflet was nearly transparent, and at 7 o'clock, from a surgeon's view, was a 4- to 5-mm circular hole; there were no vegetations. Pathological examination of the edge of this tissue and culture later revealed no serious abnormalities. A 31-mm porcine xenograft was implanted, leaving the valve intact, except for a small biopsy site at the edge of the lesion. The cross-clamp time was 37 minutes, the perfusion time 67 minutes. The patient was discharged from the hospital 1 week after the operation.

Eight months postoperatively the patient's left ventricular ejection fraction (by multigated acquisition) was 0.42. His left ventricular angiogram demonstrated mild hypokinesis. His catheterization pressures were low but normal (Table 1) with a cardiac output of 6.5 L/min. His resting electrocardiogram was read as probable old septal infarction. On exercise treadmill test he was able to attain a heart rate of 150 beats/min and a blood pressure of 146/96 mm Hg, with a total time of 16.4 minutes, attaining 1.75 minutes of stage IV of a modified Bruce protocol (12 to 13 METS). The exercise electrocardiogram suggested an ischemic change. Clinically, he is in functional class I. Captopril and ethacrynic acid have been eliminated from his medical regimen and long-acting nifedipine (30 mg four times daily) has been added.

Comment

It is not known whether the nicely punched out hole in this patient's posterior mitral leaflet resulted from endocarditis at the time of his staphylococcal mediastinitis, but this is considered to be the best possibility. This, in addition to what appears to have been a progressive decrease in diastolic function of his heart leading to increasing mitral regurgitation, seemed to have caused his symptoms. His clinical course was one of fairly rapid deterioration; given this rapid course, and his unhappi-

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Table 1. Postoperative Studies

Studies After Transplantation	Time in Years						11/14/90 8 Mo After MVR
	1	2	3	4	5	6	
Cardiac catheterization pressures (mm Hg)							
$\overline{\text{RA}}$	5	8	6	6	9	10	5
RV	23/5	31/8	25/6	28/6	32/8	36/10	25/5
PA/$\overline{\text{PA}}$	23/10/17	30/15/20	25/12/16	26/12/18	26/14/20	30/16/22	24/7/15
PAW	12	16	10	14	14	16	8
LV	110/20	126/16	125/12	125/14	142/12	90/18	100/2
AO/$\overline{\text{AO}}$	115/80/95	126/85/103	120/80/42	125/90/105	139/98/118	95/65	100/80
Coronary arteries	Normal	Normal	Normal	Normal	Normal	Normal	Normal
CO (L/min)	5	5.9	4.7	8.3	8.7	7.3	6.5
EF	0.70	0.67	0.70	Normal	NC	0.60	Mild hypokinesis
LVgram	1–2+ MR	2+ MR	NC	NC	2–3+ MR	2+ MR	No MR
MUGA EF	0.58	0.62	0.70	0.73	0.61	0.58	0.42
ETT							
Exercise time (min)	13	16	15	15	12.3	15	16
ECG	Normal	Normal	Normal	Ischemic response	Ischemic response	Ischemic response	Suggested ischemic response
ECG at rest	Normal	Normal	Normal	Normal	Normal	Normal	LA enlargement, ?old septal MI
Echocardiogram							
LV wall	Normal		Concentric LVH		Concentric LVH		Mild concentric LVH
LV systolic dimension (mm)	21		25		30		35
LV diastolic dimension (mm)	40		48		47		50
MR	1–2+		2+		1+		0
BUN (mmol/L urea)	9.3	11.4	12.5	8.6	13.9	. . .	7.1
Serum creatinine (μmol/L)	124	124	141	115	168	. . .	124
Cyclosporine dose (mg/d)	300	300	240	260	200	200	200
Prednisone (mg/d)	10	15	15	15	5	5	5
Azathioprine (mg/d)	. . .	. . .	. . .	. . .	75	75	75
Ethacrynic acid (mg/d)	50	50	50	50	50	50	Procardia XL, 30 mg
Captopril (mg/d)	. . .	25	25	25	50	5	

AO/$\overline{\text{AO}}$ = aortic/mean aortic; BUN = blood urea nitrogen level; CO = cardiac output; ECG = electrocardiogram; EF = ejection fraction from left ventriculogram; ETT = exercise tolerance test; LA = left atrial; LV = left ventricular; LVgram = left ventriculogram; LVH = left ventricular hypokinesis; MI = myocardial infarction; MR = mitral regurgitation; MUGA EF = ejection fraction from nuclear multigated acquisition study; NC = not completed; PA/$\overline{\text{PA}}$ = pulmonary artery/mean pulmonary artery; $\overline{\text{PAW}}$ = mean pulmonary artery wedge; $\overline{\text{RA}}$ = mean right atrial; RV = right ventricular.

ness with a seriously limited lifestyle, we proceeded with valve replacement rather than placing the patient on the list for retransplantation. It appears that he has made a substantial clinical improvement, and he continues to have restrictive cardiac disease, as is often seen in chronic cardiac transplant recipients. The fact that he is working full time at hard labor and feels markedly improved suggests that we have accomplished our immediate goal of survival from valve replacement without complication. We may have delayed what appears to be a course leading toward eventual retransplantation.

Although this gain is not spectacular, it does keep this patient off the transplant list, theoretically providing a heart for some other potential recipient, and it does return our patient to what seems to be a tolerable existence. We thus have obtained a level of palliation and extended the period of function of his cardiac graft.

We are convinced from this experience and one previous experience in a patient 9 years after transplantation who benefited from coronary artery bypass grafting [1] that repair and revascularization of the transplanted heart, although rarely done, may in select cases be reasonable and beneficial. We would therefore encourage those with suitable patients to proceed in this direction.

Reference

1. Copeland JG, Butman SM, Sethi G. Successful coronary artery bypass grafting for high-risk left main coronary artery atherosclerosis after cardiac transplantation. Ann Thorac Surg 1990; 49:106–10.

REVIEW OF RECENT BOOKS

Diagnosis of Diseases of the Chest, Vol 4, 3rd Edition

By Robert G. Fraser, J. A. Peter Pare, P. D. Pare, Richard S. Fraser, and George P. Genereux
Philadelphia, W.B. Saunders, 1991
912 pp, illustrated, $90.00

Reviewed by Stephanie M. Levine, MD

Diagnosis of Disease of the Chest, volume 4, third edition, continues to be one of the outstanding reference textbooks of thoracic diseases. The textbook is a composite of etiologies, pathogenesis, pathology, physiology, clinical characteristics, radiology, and prognosis of chest diseases. As in the past, it does not cover therapeutic modalities.

Consisting of 912 pages, volume 4 is divided into eight chapters: Drug- and Poison-Induced Pulmonary Disease, Diseases of the Thorax Caused by External Physical Agents, Metabolic Pulmonary Disease, Pulmonary Disease of Unknown Origin, The Pleura, Disease of the Mediastinum, Diseases of the Diaphragm and Chest Wall, and Respiratory Disease Associated With a Normal Chest Roentgenogram. The chapter "Diseases of the Thorax Caused by External Physical Agents" includes sections on nonpenetrating trauma of the lungs, the pleura, the mediastinum, the diaphragm, and the chest wall as well as penetrating trauma of the thorax. All chapters are internally referenced and current. This volume also contains a useful appendix, which categorizes chest diseases and processes by 17 different radiographic appearances. Examples of these categories include: cystic and cavitary disease; solitary pulmonary nodules less than 3 cm in diameter; diffuse pulmonary disease with a predominantly nodular, reticular, or reticulonodular pattern; hilar and mediastinal lymph node enlargement; and mediastinal widening. A composite index of all references by author is included with the location of each citation in the volume, as well as a cumulative subject index of all four volumes.

In comparison with previous editions, the authors have expanded on the pathophysiology of the diseases to include both gross and microscopic examples, although not consistently. This edition surpasses the previous editions with the use of more advanced radiographic illustrations, particularly advanced-generation computed tomography and occasional magnetic resonance imaging. Furthermore, there are new comprehensive chapters on drug- and poison-induced disease, as well as metabolic pulmonary disease.

Although this text is not for general thoracic surgery reading, its purpose as reference material for all levels of thoracic surgery as a link between pulmonary medicine, pulmonary radiology, pulmonary pathology, and thoracic surgery is unsurpassed. The chapters on penetrating and nonpenetrating chest trauma and on the mediastinum will be particularly useful to those in the field of thoracic surgery.

San Antonio, Texas

Aortic Atresia With Normal Left Ventricle

Alain Serraf, MD, Jacqueline Bruniaux, MD, Jérôme Lebidois, MD,
François Lacour-Gayet, MD, Jean Kachaner, MD, and Claude Planche, MD

Department of Pediatric Cardiac Surgery, Marie-Lannelongue Hospital, Paris, France

A case of single-stage repair of aortic atresia with normal-sized left ventricle and ventricular septal defect in a neonate is reported. The surgical procedure included rerouting of the left ventricular bloodstream to the pulmonary artery through the ventricular septal defect and connection of the pulmonary trunk to the aortic arch. The right ventricular outflow tract was then reconstructed with an extracardiac valved conduit. Three years after the initial operation, replacement of the valved conduit was performed uneventfully. The clinical status of the child is very satisfactory.

(Ann Thorac Surg 1991;51:1017–9)

Aortic atresia is generally a component of hypoplastic left heart syndrome; however, in a small proportion of patients (5% to 7%) [1–4] a moderate or large interventricular communication will be found. When this occurs, the left ventricle will be more fully developed and may even approach normal size. Operation that may correct this anomaly by reconstruction of systemic and pulmonary pathways, each with its own ventricular chamber, has been successfully performed as a two-stage repair [5–8] and recently as a single-stage repair in neonates [9].

We report a similar case of aortic atresia with fully developed left ventricle, normal mitral valve, and ventricular septal defect in a neonate who underwent single-stage repair at Marie-Lannelongue Hospital. Midterm follow-up of 3 years is reported.

A 15-day-old girl was referred to our department for surgical repair of a truncus arteriosus. She was born after an unremarkable pregnancy with a birth weight of 2.9 kg. Shortly after birth, she was noted to have tachypnea, hepatomegaly, and systolic cardiac murmur; peripheral pulses were palpable. Chest roentgenograms showed moderate cardiomegaly and increased pulmonary vascularity. The electrocardiogram was unremarkable.

Echocardiography and angiography were compatible with diagnosis of type II truncus arteriosus; however, it was relevant to notice that no coronary arteries could be seen on the angiogram. Catheterization demonstrated right and left ventricular pressures of 100/0 mm Hg, and the descending aortic pressure was 100/60 mm Hg. Aortic saturation was 0.85.

Because her clinical status did not improve under medical therapy, she was transferred to the operating room on May 15, 1987. After sternotomy, anatomy did not reveal a truncus arteriosus but an aortic atresia with an ascending aorta 2.5 mm in diameter. Cardiopulmonary bypass was instituted between the pulmonary trunk and both venae cavae. During cooling, the left ventricle was tunnelized through a right ventriculotomy to the pulmonary artery through the ventricular septal defect. Aortic repair was performed under deep hypothermia and circulatory arrest. The pulmonary artery was divided immediately proximal to its bifurcation, and the ductus arteriosus was ligated and divided at its junction with the aorta. The aorta was largely opened in the arch and transected proximal to the innominate artery, allowing a Lecompte maneuver. A 10-mm nonvalved, woven Dacron conduit was inserted between the proximal pulmonary trunk and the aortic arch. Cardiopulmonary bypass was then reinstituted, and during warming a Carpentier-Edwards 12-mm extracardiac conduit was inserted between the right ventricle and the pulmonary artery bifurcation (Fig 1).

The patient required ventilatory support for 6 days, and her condition gradually stabilized. She was discharged on the 20th postoperative day. Her clinical status was perfectly stable until November 1989, when a systolic murmur was noted and echocardiography showed stenosis in the right ventricle to pulmonary artery conduit. She underwent catheterization with angiography that showed normal left ventricular anatomy and coronary supply (Fig 2) and an unobstructed systemic pathway (Fig 3). Right ventricular outflow tract angiography demonstrated stenosis at the valvar level and at the origin of the right pulmonary artery. The right ventricle to pulmonary arterial gradient was 60 mm Hg.

On June 5, 1990, she underwent replacement of the right ventricle to pulmonary artery conduit with patch angioplasty of the right pulmonary artery. Unfortunately, an adequate sized homograft was not available and a Carpentier-Edwards 16-mm conduit was inserted. The postoperative course was uneventful, and she was discharged on the tenth postoperative day.

Comment

Aortic atresia with an adequately developed left ventricle and mitral valve has been recognized as an anatomical and clinical entity [1, 3–5]. Despite these features, ulti-

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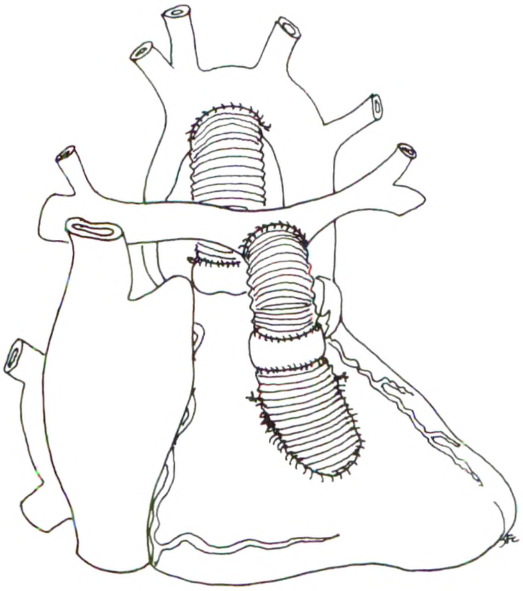

Fig 1. At completion of the repair, the right ventricular outflow tract is reconstructed with a valved conduit between the right ventriculotomy and the pulmonary artery bifurcation.

mate survival depends on patency of the ductus arteriosus for systemic and coronary perfusion. The size of the atrial septal defect is not as relevant as in hypoplastic left heart syndrome because oxygen mixing can be satisfactorily achieved at the ventricular level.

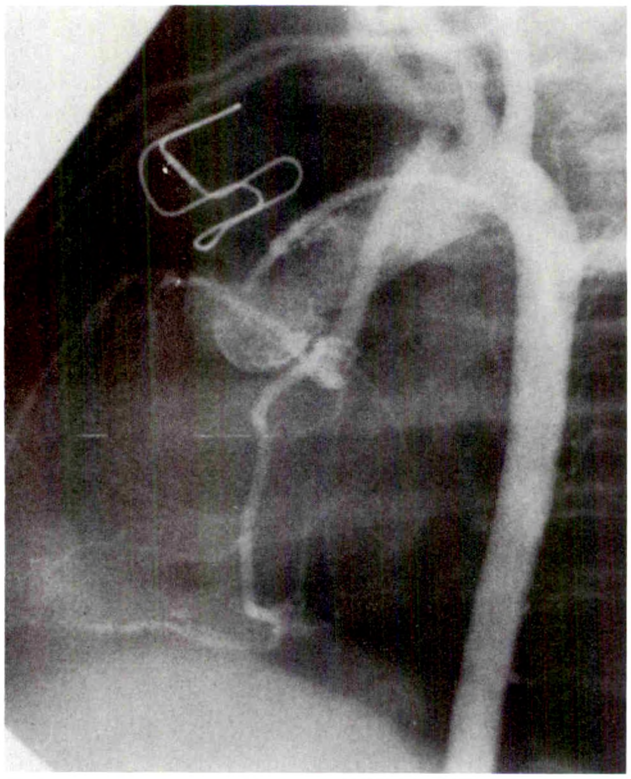

Fig 2. Left anterior oblique view showing the primitive tiny ascending aorta providing two coronary arteries.

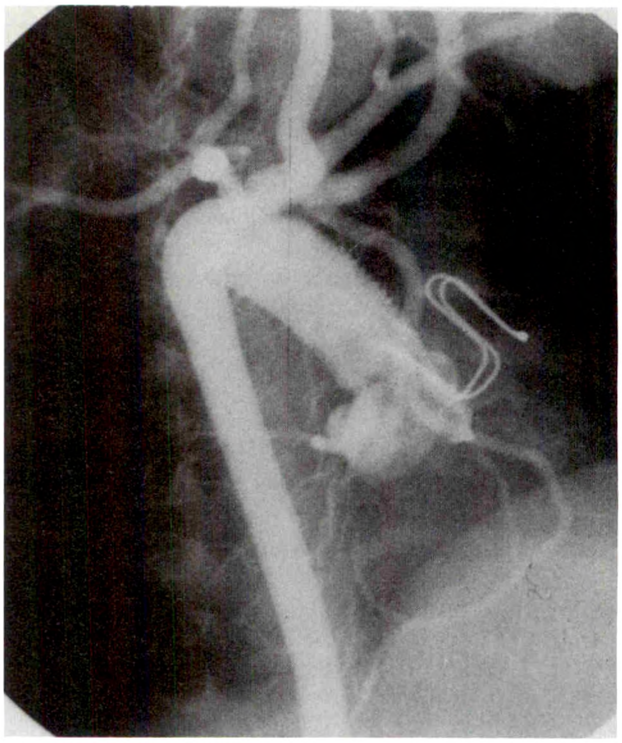

Fig 3. Angiography demonstrating an unobstructed systemic pathway reconstruction.

Although numerous centers remain reluctant to recommend operation for newborns with hypoplastic left heart syndrome, aortic atresia with normal-sized left ventricle related to the presence of a ventricular septal defect provides the opportunity for a reparative procedure leading to two functional ventricles. Successful early surgical palliation subsequently followed by complete repair has been reported [7, 8]. The first stage includes the establishment of a stable systemic blood flow using a conduit between the pulmonary artery and aorta with pulmonary artery banding. Later on, the second stage procedure is performed and includes closure of the ventricular septal defect, ligation of the pulmonary artery to aorta conduit, release of pulmonary artery banding, and insertion of a left ventricular apex to thoracic aorta conduit.

In 1979, Thiéne and associates [4] proposed a repair that includes tunneling the left ventricle through the ventricular septal defect to the pulmonary artery trunk, which communicates by means of a surgically enlarged ductus arteriosus with the aorta; the pulmonary artery branches are separated from the trunk and connected to the right ventricle using an external valved conduit. Recently, Austin and colleagues [9] reported 4 cases of single-stage repair in neonates using the Thiéne procedure. This procedure was applied in our case, but reconstruction of the right ventricular outflow tract was performed after a Lecompte maneuver. This patient then underwent replacement of the right ventricle to pulmonary artery bifurcation conduit and was discharged on the tenth postoperative day.

In conclusion, aortic atresia with normal-sized left ventricle is a malformation that has to be distinguished from the hypoplastic left heart syndrome because it is amenable to ventriculoaortic repair in most cases.

References

1. Moodie DS, Gallen WJ, Friedberg DZ. Congenital aortic atresia. J Thorac Cardiovasc Surg 1972;63:726–31.
2. Roberts WC, Perry LW, Chandra RS, Myers GS, Shapiro SR, Scott LP. Aortic valve atresia: a new classification based on necropsy study of 73 cases. Am J Cardiol 1976;37:753–6.
3. Freedom RM, Dische MR, Rowe RD. Conal anatomy in aortic atresia, ventricular septal defect, and normally developed left ventricle. Am Heart J 1977;94:689–98.
4. Thiéne G, Gallucci V, McCartney FJ, Del-Torso S, Pellegrino PA, Anderson RH. Anatomy of aortic atresia. Cases presenting with a VSD. Circulation 1979;59:173–8.
5. Freedom RM, Williams WG, Dische MR, Rowe RD. Anatomical variants in aortic atresia. Potential candidates for ventriculo-aortic reconstitution. Br Heart J 1976;38:821–6.
6. Norwood WI, Kirklin JK, Sanders SP. Hypoplasic left heart syndrome: experience with palliative surgery. Am J Cardiol 1980;45:87–91.
7. Norwood WI, Stellin GJ. Aortic atresia with interrupted aortic arch. J Thorac Cardiovasc Surg 1981;81:239–44.
8. Duffy CE, Muster AJ, De Leon SY, et al. Successful surgical repair of aortic atresia associated with normal left ventricle. J Am Coll Cardiol 1983;1:1503–6.
9. Austin EH, Jonas RA, Mayer JE, Castaneda AR. Aortic atresia with normal left ventricle. Single stage repair in the neonate. J Thorac Cardiovasc Surg 1989;97:392–5.

Notice From the American Board of Thoracic Surgery

The part 1 (written) examination will be held at the Hyatt-Regency, Dallas Fort Worth Airport, Dallas TX, on February 16, 1992. The closing date for registration is August 1, 1991.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

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New Technique of Esophageal Exclusion for Chronic Esophageal Perforation

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A new technique of near-total esophageal exclusion was used successfully in the treatment of 2 patients with chronic thoracic esophageal perforation and continuing sepsis. The most striking point of this technique is the use of cervical T-tube esophagostomy with the lower arm of the T tube circumfixed by chromic catgut tie to prevent swallowing of saliva. Whereas most of the previously reported procedures of cervical esophageal diversion require subsequent esophageal reconstruction, this technique is simple and effective and does not require a second operation.

(Ann Thorac Surg 1991;51:1020–2)

Exclusion of esophagus is one of the effective methods in the treatment of chronic esophageal perforation [1]. For diverting saliva, different kinds of techniques have been advocated [1]. Nevertheless, most of the diverting techniques need a second-stage reconstruction, which usually prolongs hospitalization and potentially increases the operative risk. Gunning and Kingsnorth [2] reported on the usefulness of a cervical T-tube esophagostomy with nasogastric tube suction for drainage of swallowed saliva, in which a second operation was not required. But an additional endoscopic sclerosing therapy was needed for healing of the perforation hole, mainly because the diversion was incomplete [2].

A new technique of esophageal exclusion using a cervical T tube with modification was designed for chronic esophageal perforation. We used this technique successfully in the treatment of 2 patients with persisting septic symptoms and signs in whom conservative treatment had failed. The operative technique and the clinical features of these 2 patients are presented.

Operative Technique

The technique of esophageal exclusion is illustrated in Figure 1, which includes chest tube drainage of purulent effusion, draining tube gastrostomy, feeding tube jejunostomy, and cervical T-tube esophagostomy. The rubber T tube (diameter, 1.0 cm) was modified to have a short upper arm (0.5 cm) and longer lower arm (3 to 4 cm). The lower opening was closed by 2-0 silk suture ligature, and the lower arm was circumferentially fixed to the esophageal wall with 1-0 chromic catgut tie to prevent drainage of saliva to the lower esophagus. The cervical T-tube esophagostomy was left in place for 2 to 3 weeks until the esophageal perforation was healed as proved by esophagogram. The T tube could be pulled out easily because the catgut ligature had gradually lost its tensile strength. The esophagostomy wound healed within 2 days without esophageal stricture.

Case Reports

Patient 1

The first patient is a 12-year-old girl who had esophageal variceal bleeding due to chronic hepatitis with cirrhosis and in whom high fever (40°C) and chest pain developed 1 day after five serial endoscopic sclerotherapies within a month. A chest roentgenogram taken 3 days later showed massive left pleural effusion with air-fluid level (Fig 2). A chest tube was inserted, and more than 300 mL of purulent effusion was drained each day for 8 consecutive days. An esophagogram examined at that time showed extravasation of dye at the lower esophagus (Fig 3). A bacterial culture of pus had growth of *Streptococcus intermedius* and *Klebsiella pneumoniae*. In spite of parenteral antibiotics, intravenous nutrition, and continuing chest tube drainage, the patient still had high fever every day, and her general condition became worse.

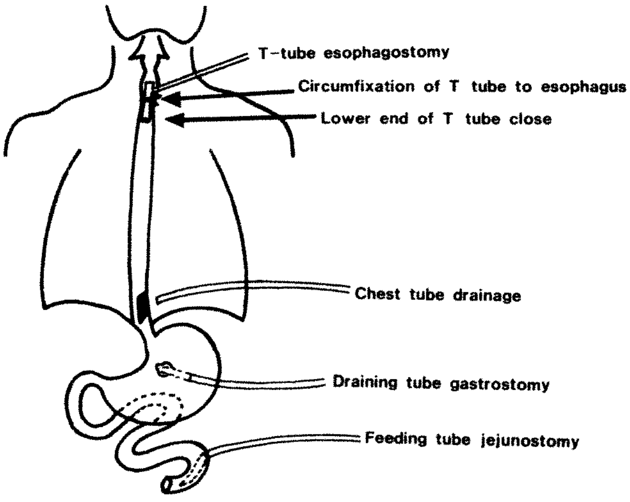
T-tube esophagostomy
Circumfixation of T tube to esophagus
Lower end of T tube close
Chest tube drainage
Draining tube gastrostomy
Feeding tube jejunostomy

Fig 1. The surgical technique of near-total esophageal exclusion.

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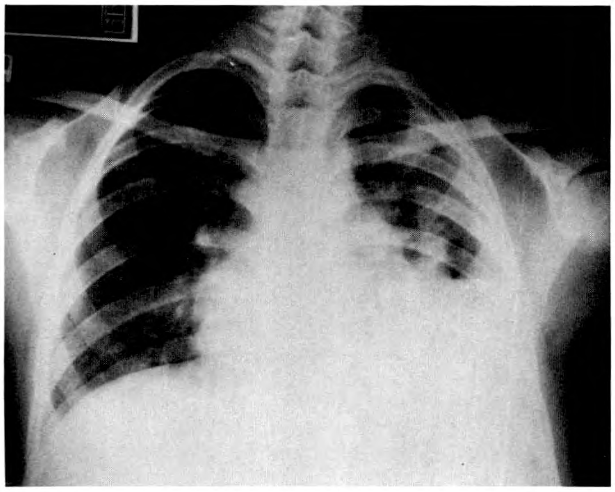

Fig 2. Chest roentgenogram of patient 1 shows left pneumopyothorax.

She was operated on using the esophageal exclusion technique 14 days after the onset of symptoms. Two days after the procedure, the patient became afebrile and the amount of chest tube drainage became scanty. She had an uneventful recovery. A follow-up esophagogram 1 month after operation showed good healing of esophageal perforation. No stricture could be found in the cervical esophagus (Fig 4).

Patient 2

A 61-year-old man had misswallowed a chicken bone and underwent endoscopic removal of the foreign body. Chest pain, high fever, and subcutaneous emphysema developed 1 day later. Esophagoscopic examination showed an esophageal perforation at the middle thoracic esophagus with pus gushing out during respiration. He was treated by nasogastric decompression, parenteral antibiotic, and intravenous nutrition, but he still had spiking fever every day. He was operated on 7 days after esophageal perforation using the esophageal exclusion technique. The patient became afebrile 2 days after the procedure. The T tube was removed 2 weeks later, and the esophagostomy wound healed in 2 days. He resumed oral intake smoothly. An esophagogram taken 2 months later demonstrated a smooth esophageal passage.

Comment

Miscellaneous techniques of exclusion of esophagus are used in the treatment of esophageal perforation [1]. Nevertheless, most of them necessitate a second-stage operation for reconstruction. Our technique is similar to that reported by Ergin and associates [3] in 1980. They used cervical tube esophagostomy and esophageal tape restriction at the lower level of esophagus for drainage of saliva; but still, a second operation was required for removal of the esophageal tape after healing of the esophageal perforation. Our technique uses a T tube for a splint and 1-0 chromic catgut tie restriction to prevent drainage of saliva to the lower esophagus. Because the catgut tie will gradually lose its tensile strength and be absorbed in 2 or 3 weeks [4], the esophageal T tube can be removed easily after this period, which is usually good enough for healing of the perforation hole.

One potential risk of our technique is the development of esophageal stricture at the location of the catgut tie. But using the lower arm of the T tube for splint of the catgut tie made the possibility of stricture formation very small. Neither of the patients in whom we used the technique of esophageal exclusion had esophageal stricture at the neck level, as proved by esophagograms performed 1 and 2 months later, respectively.

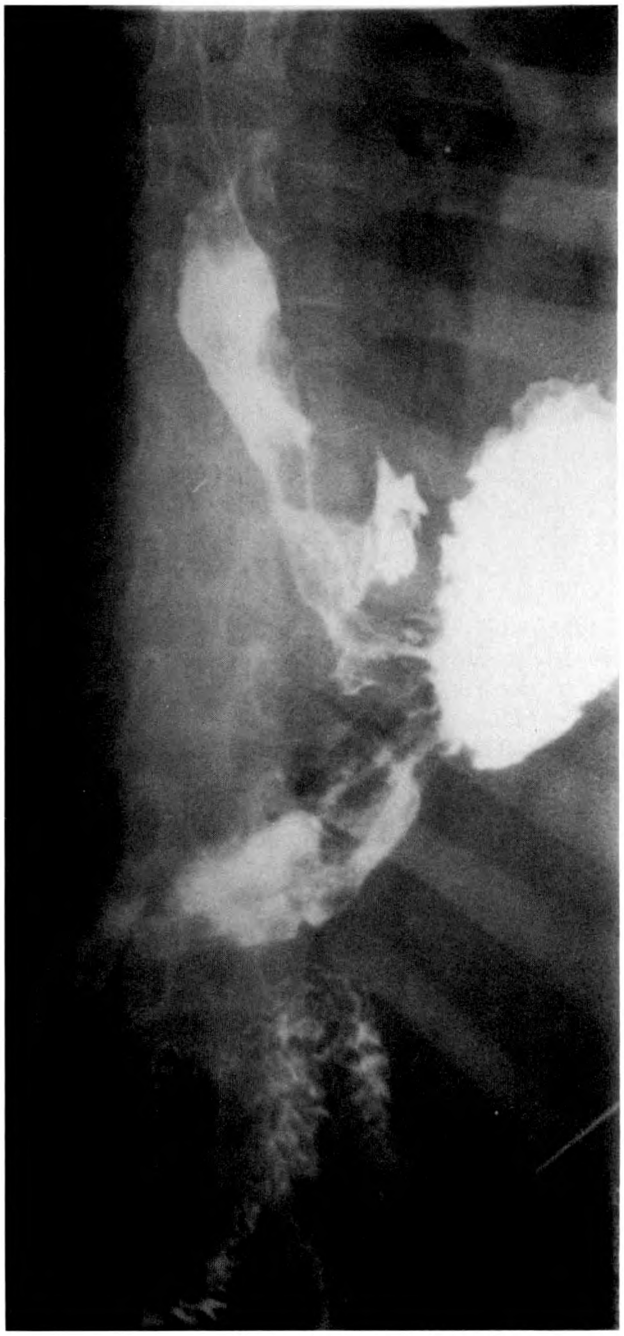

Fig 3. Esophagogram of patient 1 taken before operation demonstrates extravasation of dye at the lower esophagus.

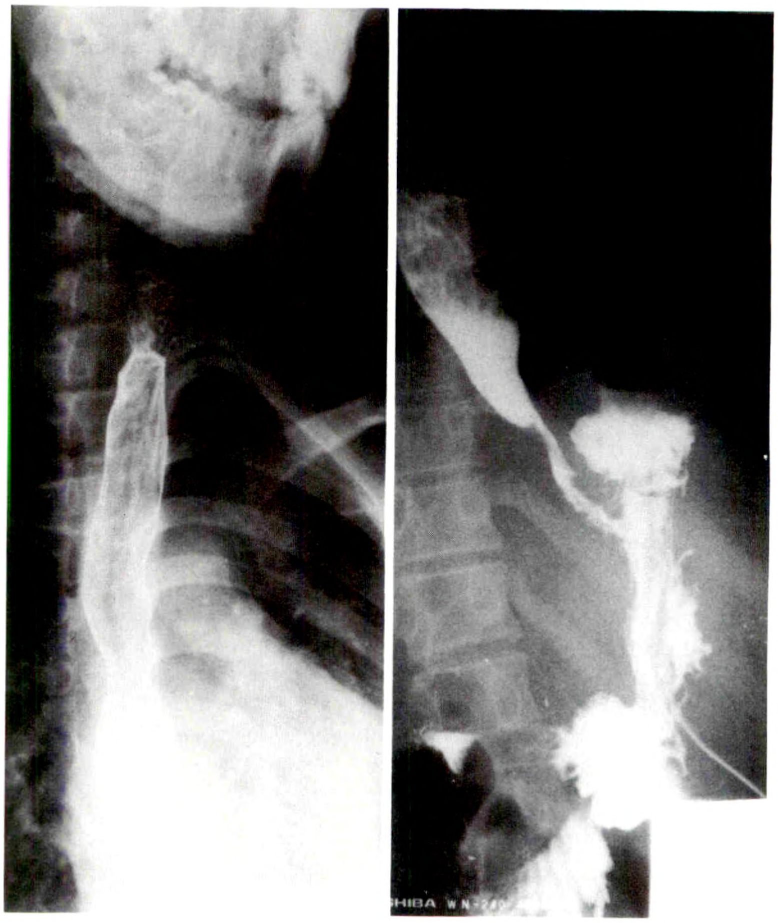

Fig 4. Esophagogram of patient 1 taken 1 month after operation shows no cervical esophageal stricture (left) *and good healing of lower esophageal perforation* (right).

When the perforation hole of the esophagus is large or severely infected, a longer period of esophageal exclusion will be expected for healing of the perforation. Then a longer duration absorbable tie such as Dexon, instead of chromic catgut, is suggested for fixation of the lower arm of the T tube. Using a nonabsorbable tie such as silk or Prolene to substitute for catgut, our technique might be useful in the conditions that need prolonged drainage of swallowed saliva for palliation, such as inoperable malignant tracheoesophageal fistula.

References

1. Goldstein LA, Thompson WR. Esophageal perforation: a 15 year experience. Am J Surg 1982;143:495–503.
2. Gunning AJ, Kingsnorth A. Treatment of chronic esophageal perforation with special reference to an endoscopic method. Br J Surg 1979;66:226–9.
3. Ergin MA, Wetstein L, Griepp RB. Temporary diverting cervical esophagostomy. Surg Gynecol Obstet 1980;151:97–8.
4. Haxton HA. The absorption of catgut in human abdominal wounds. Br J Surg 1963;50:534–6.

Technique and Pitfalls of Retrograde Continuous Warm Blood Cardioplegia

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The recent development of normothermic myocardial preservation and systemic perfusion during bypass has questioned the fundamental need for hypothermia during cardiac operations. The antegrade technique of almost continuous perfusion by the aortic root and vein grafts has been supplemented by continuous normothermic blood cardioplegia through the coronary sinus. Recently, great interest has been shown in this technique. It is important to describe the method in detail along with its potential shortcomings and dangers. This communication describes the technical details, pitfalls, and shortcomings of retrograde continuous warm blood cardioplegia.

(Ann Thorac Surg 1991;51:1023–5)

The retrograde continuous warm blood cardioplegia (RCWBC) technique is similar for all types of cardiac procedures, as recently reported [1]. Standard cardiopulmonary bypass techniques are used with cannulation of the ascending aorta and single- and double-stage venous cannulas. In mitral valve replacement both venae cavae are cannulated but not snared. Before commencement of normothermic bypass, the coronary sinus cannula is usually inserted transatrially, as previously reported [2]. Placement of the cannula before cardiopulmonary bypass is easier as the coronary sinus ostium is distended. Placement has been successful in 96% of our cases [3]. Its position is confirmed by finger palpation with the hand behind the heart in the atrioventricular groove. If the patient's condition is unstable, partial bypass is instituted and then the coronary sinus is cannulated. The pursestring in the atrium is made close to the coronary sinus, because there is a tendency for displacement of the cannula, but should be on right atrial tissue and not on the coronary sinus opening to the right atrium. The surgeon then should inspect the heart for possible anomalies, such as a left superior vena cava draining into the coronary sinus. Although rare, this anomaly may preclude the use of this technique, and if missed, may cause serious problems with lack of cardioplegic delivery to the heart.

The heart is arrested using high-potassium blood cardioplegia, employing four portions of blood to one portion of high-potassium Fremes solution (D5W, 500 mL; KCl, 50 mEq; $MgSO_3$, 9 mEq; Tromethamine, 6 mEq; CDP solution, 10 mEq; osmolality ≈ 425 mOsm/L; pH ≈ 7.95; total volume ≈ 557 mL). As soon as diastolic arrest occurs the perfusion system is switched to the retrograde cannula. Some surgeons prefer to deliver 1 L of cardioplegia antegradely before switching to the retrograde route, but this is not necessary. Low-potassium Fremes solution (same composition as high-potassium Fremes solution but KCl = 30 mEq/L) is delivered in the same proportion at a maximum mean pressure of 40 mm Hg, measured at the side port of the coronary sinus cannula. Cardioplegic delivery should not exceed 250 mL/min. The infusion pressure and flows are constantly monitored by the perfusionist during the procedure. Should electrical activity occur, additional high-potassium cardioplegia (usually 200 to 300 mL of high-potassium Fremes solution) is infused retrogradely until arrest occurs. Alternatively a higher maintenance potassium concentration may be employed (40 mEq/L). Electrical activity has recurred after arrest in approximately 10% of our cases. Before aortic unclamping, cardioplegia is discontinued and the cannula is removed if no rearrest is planned. Alternatively the cannula may be opened to air. This occurs in case of mitral valve repairs when the surgeon may elect to perform further repair or replacement. Our clinical experience so far indicates that rearrest is safe with crystalloid cardioplegia [4] and with RCWBC.

Antegrade Arrest

Although we have on occasion infused continuous warm blood cardioplegia retrogradely to arrest the beating heart, we have not consistently employed this technique because of the lengthy time to diastolic arrest. Even in case of severe aortic insufficiency, initial antegrade cardioplegia is administered until arrest occurs, or the aorta is opened and the coronary ostia are cannulated directly for antegrade arrest.

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Position of the Coronary Sinus Cannula

The technique of insertion has evolved as described by Drinkwater and colleagues [2], with the exception that we advance the cannula as far as it goes into the coronary sinus. This is the case even in hypertrophied ventricles (left or right). Failure to do so, especially in complex procedures, may cause unrecognized displacement of the cannula into the right atrium, leaving the heart ischemic and normothermic. This was the cause of death in at least 1 patient in our initial experience, whose catheter displaced during the procedure. Although unproven, we believe that the mechanism of myocardial protection through the coronary sinus in humans is different than in animals. Although conventional methods of cardioplegia administration relied on cold cardioplegia and topical cooling, this method relies on continuous perfusion and chemical arrest, not hypothermia [5].

How then can one be assured of the position of the catheter? Meticulous care in its insertion and with the atrial pursestring suture and placement of the catheter as far as possible into the coronary sinus are two important concepts. This is particularly important in mitral valve operations, in which retraction of the interatrial septum may dislodge the cannula. Although palpation may seem 100% reliable, at times it is difficult to know by palpation alone where the catheter is, especially in a fatty heart. This can cause undue delay in or lack of cardioplegic delivery. In patients who undergo aortic valve replacement, blood can be seen coming from both coronary ostia, or from the coronary arteries when bypass grafting is performed. The desaturated blood can be seen emanating from the left ventricle and aortic root in mitral valve replacement or repair. We do not recommend discontinuation of warm blood cardioplegia in hypertrophied hearts, although we have done so for brief periods of time in hearts undergoing coronary bypass grafting [5].

Such qualitative assessment, however, is not foolproof. Pressure monitoring of the side port of the cannula at present remains the most reliable method of surveillance for catheter position. An abrupt change in pressure, ie, from between 30 and 40 mm Hg to between 1 and 4 mm Hg or negative pressures, indicates catheter displacement. The catheter at this time should be checked and positioned appropriately to ensure cardioplegic delivery. By filling up the right atrium (with partial venous occlusion) and observing pressure changes in the coronary sinus catheter, the surgeon can determine whether the catheter has been displaced into the right atrium. (The pressure in the catheter port will increase with filling of the right atrium.) This is not true with some catheters in which coronary sinus occlusion may be inadequate, and therefore any decrease in coronary sinus pressure should result in immediate inspection of catheter position and the degree of balloon inflation.

Catheter position can also be monitored during RCWBC by measuring myocardial temperatures (37°C when cardioplegia is delivered and room temperature when not). We are currently investigating the use of a needle oxygen tension probe that will allow monitoring of instantaneous myocardial oxygenation.

The heart becomes pale when the catheter is out of the coronary sinus. Distention and filling of the great cardiac veins with pink blood implies good catheter position, whereas empty and dark veins usually imply displacement. We rely heavily on this technique, although there is no guarantee of adequacy of cardioplegic delivery.

How to Deal With Flooding of Blood in the Operative Field

As we have become more confident and comfortable with warm heart operations, it has become apparent that short periods of ischemia (10 to 15 minutes) are well tolerated by the arrested heart [3]. This is presumably because of the finding that oxygen consumption of warm- and cold-arrested hearts are not clinically significantly different [6, 7]. Current research is underway to determine the safety of intermittent warm cardioplegia. In coronary operations blood in the operative field is dealt with by local irrigation with warm saline solution, insertion of a probe into the coronary artery, snaring of the coronary artery, or discontinuation of cardioplegia for short periods of time. These techniques are not ideal. Recently, we [8] have employed a stream of oxygen at 10 to 12 L/min to enhance visualization of the coronary anastomoses.

How Much Cardioplegia Should the Surgeon Administer?

There is no firm basis as yet to indicate what flow rates should be administered to the warm, chemically arrested heart. In our clinical practice it ranges from 40 to 150 mL/min in hearts with coronary artery disease and up to 250 mL/min in hypertrophied hearts. It is hoped that soon we will be able to predict what volumes are required on an individual basis through clinical trials and animal research. Because the solution is basically blood with low potassium concentrations, we tend to administer more than what we think is needed, especially in hypertrophied hearts, to have a large safety margin.

Use in Combined Valvar and Coronary Operations

This technique is particularly suitable to combined valvar and coronary operations. One of the attractions of RCWBC is that the order of the procedure does not matter. For example, in critical left main stenosis combined with aortic valve disease, we have performed a valve replacement before coronary bypass. The reverse may also be done. Venous effluent through the coronary ostia does not seem to impair the technical aspects of aortic valve operation, as the volume of blood exiting by the coronary ostia is small. Indeed, the adequacy of left and right ventricular perfusion by the coronary sinus is constantly assured by the return of the desaturated blood.

Is Potassium a Problem at the End of the Procedure?

Clinical data indicate that potassium is not a problem [3, 5]. Should the potassium level become elevated during the operation, the problem may be treated by maintaining urine output with furosemide or employing glucose, insulin, and bicarbonate. Rarely has this been a serious problem. In fact, with warm perfusion the ability of the body to cope with the potassium loads may be enhanced when compared with cold heart operations. If a long cross-clamp time or other causes for hyperkalemia are anticipated, 10 to 20 mg of furosemide given into the pump at the beginning of RCWBC may be appropriate.

Injury to the Coronary Sinus

Our experience now nears 300 patients over 4 months using this technique. No injuries to the coronary sinus have occurred. This seems to be the experience of others who have used this method as well. We have employed the Research Medical Retroplegia Cannula as described by Drinkwater and colleagues [2].

Right Ventricular Preservation and Postoperative Problems

The key question that has not been completely answered is the extent of right ventricular preservation during RCWBC. The full answer to this question will require further clinical experience and controlled clinical trials. To date we have performed all valvar and combined procedures using this method, irrespective of the degree of ventricular hypertrophy and pulmonary artery pressures. There has not been a single case of right ventricular failure [3]. Further basic research is under way at our laboratories using models of left and right ventricular hypertrophy [9, 10] to answer this important question. After cross-clamp removal, approximately 96% of hearts revert to spontaneous sinus rhythm. Junctional rhythm may occasionally occur; however, it is rare for pacing to be necessary postoperatively. Occasionally, patients may require pacing to come off cardiopulmonary bypass; however, once potassium levels decrease to a more normal range, they return to sinus rhythm.

Summary

In summary, RCWBC is a new concept in myocardial protection [3], offering many advantages over the antegrade method [5]. These include the elimination of cannulas in the coronary ostia during valvar operations, elimination of left ventricular distention due to aortic insufficiency during retraction of the heart, and elimination of concerns related to the distribution of cardioplegia due to severe coronary artery stenosis. As with any technique, caution is required during its use, and certain principles of cardioplegic delivery must be followed (monitoring of infusion pressure and surveillance of catheter position during infusion) to ensure appropriate delivery. Used appropriately, the method appears to be safe and effective. Additional studies, however, are necessary to document any improvement over traditionally employed techniques of myocardial protection.

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References

1. Salerno TA. Continuous blood cardioplegia: option for the future or return to the past [Abstract]? J Mol Cell Cardiol 1990;22(Suppl 5):549.
2. Drinkwater DC, Laks H, Buckberg GD. A new simplified method of optimizing cardioplegic delivery without right heart isolation. J Thorac Cardiovasc Surg 1990;100:56–64.
3. Salerno TA, Houck JP, Barrozo CAM, et al. Retrograde continuous warm blood cardioplegia: a new concept in myocardial protection. Ann Thorac Surg 1991;51:245–7.
4. Salerno TA, Charrette EJP, Chiong MA. Is cardioplegic re-arrest safe? Can J Surg 1981;24:483–4.
5. Lichtenstein SV, Ashe KA, ElDalati H, et al. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
6. Buckberg GD, Brazier JR, Nelson RL, et al. Studies of the effect of hypothermia on regional perfused beating, fibrillation, and arrested heart. J Thorac Cardiovasc Surg 1977;73:87–94.
7. Chitwood WR, Sink JD, Hill RC, et al. The effects of hypothermia on myocardial oxygen consumption and transmural coronary blood flow in the potassium-arrested heart. Ann Surg 1988;1:45–53.
8. Teoh KHT, Panos AL, Harmantas AA, et al. Optimal visualization of coronary artery anastomoses by gas jet. Ann Thorac Surg (in press).
9. Cusimano RJ, Ash KA, Abel JG, et al. A simple model of right ventricular hypertrophy. J Invest Surg 1988;1:45–53.
10. Novick RJ, Stefaniszyn HJ, Michele RP, Burdon FD, Salerno TA. Protection of the hypertrophied pig myocardium: a comparison of crystalloid, blood and Fluosol-DA cardioplegia during prolonged aortic clamping. J Thorac Cardiovasc Surg 1985;89:547–66.

The Fontan Procedure: A Historical Review

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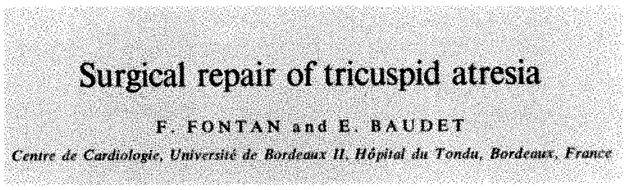
Complete bypass of the right ventricle was first performed successfully and subsequently reported by Fontan and Baudet for patients with tricuspid atresia. By eliminating congenital and surgical shunts, ventricular volume overload and pulmonary hypertension were avoided. A logical extension of its predecessor, the partial right heart bypass procedure introduced by Glenn, the Fontan operation has great application for patients with various forms of univentricular heart. It is one of the historic advances in the surgical treatment of congenital heart disease.

(Ann Thorac Surg 1991;51:1026–30)



Surgical repair of tricuspid atresia

F. FONTAN and E. BAUDET

Centre de Cardiologie, Université de Bordeaux II, Hôpital du Tondu, Bordeaux, France

In 1971, Francis Fontan and Eugene Baudet reported in *Thorax* a new operation for tricuspid atresia [TA]. The procedure, which came to bear Fontan's name, "transmits the whole vena cava blood to the lungs while only oxygenated blood returns to the left heart"[1]. In this way, the right atrium was "ventriclized." Importantly, it only applied to sufficiently well developed children with pulmonary arteries "large enough and at sufficiently low pressure to allow a cava-pulmonary anastomosis." Fontan and Baudet emphasized this was not an anatomical correction (which would require creation of a right ventricle), but a physiological correction that suppressed shunting and avoided such hazards of systemic artery to pulmonary artery shunts as pulmonary hypertension.

The procedure would eventually be recognized as a historic advance in the treatment of patients with TA. It consisted of a superior vena cava to distal right pulmonary artery anastomosis, a right atrial to proximal right pulmonary artery anastomosis, closure of atrial septal defect, ligation of main pulmonary artery, and insertion of homograft valves at the inferior vena cava–right atrial junction and right atrial to pulmonary artery anastomosis.

Before 1971, shunts (systemic artery or superior vena cava to pulmonary artery) were used for the majority of TA patients with restricted pulmonary blood flow. Alternatively, a Brock procedure [2] (enlargement of ventricular septal defect) was occasionally used, also to increase left-to-right shunting. Unfortunately, compared with the more common cyanotic disorders, shunts carried a higher operative mortality in TA patients, with Taussig and Bauersfeld [3] reporting a 26% 8-month postoperative mortality after Blalock-Taussig shunt, and Sommers and Johnson [4] finding two thirds of all patients with TA dead before 1 year of age owing to congestive failure and anoxia, whether or not operation had been performed.

The concept of a new operation for TA that eliminated shunting, both congenitally and surgically acquired, still stands as one of the major breakthroughs in congenital heart surgery. Fontan and Baudet credited Glenn's work [5, 6] with cavopulmonary anastomosis and partial right heart bypass as the conceptual stimulus for the "therapeutic basis of the operation" [1]. They attempted the operation unsuccessfully on dogs, and concluded a normal dog heart does not allow a circulation that bypasses the right heart. However, "we were of the opinion . . . a hypertrophied right atrium, as in tricuspid atresia, could supply the additional work represented by a pulmonary arterial pressure higher than the left atrial pressure, . . . but it seemed to us indispensable to provide the right atrium with valve homografts to prevent free flow between the inferior vena cava, right atrium and the pulmonary artery and, in this way, stasis in the lower half of the body and inadequate cardiac filling"[1].

In addition to Glenn's "conceptual stimulus," considerable previous evidence had suggested the right ventricle could occasionally be bypassed. As early as 1943, Starr and co-workers [7] destroyed approximately 75% of right ventricular musculature by cautery without producing an increase in peripheral venous pressure. Bakos [8] performed similar experiments, and concluded "an actively functioning right ventricle is not absolutely necessary for the maintenance of a normal pressure gradient in the arterial tree." Two other reports of extensive right ventricular damage being compatible with life appeared by 1954 [9, 10].

In a study on ventricular fibrillation, Jamison and associates [11] perfused the systemic arterial circulation with a mechanical pump as a substitute for the left ventricle. When arterial pressures were maintained between 120 and 205 mm Hg, blood could be driven through the systemic capillaries, the fibrillating right heart, the pulmonary circulation, and back to the left atrium. They concluded the left ventricle was capable of driving blood through both circulations without a functioning right ventricle. A cautionary note, however, was given by Rose and associates [12, 13], who in repeating this experiment

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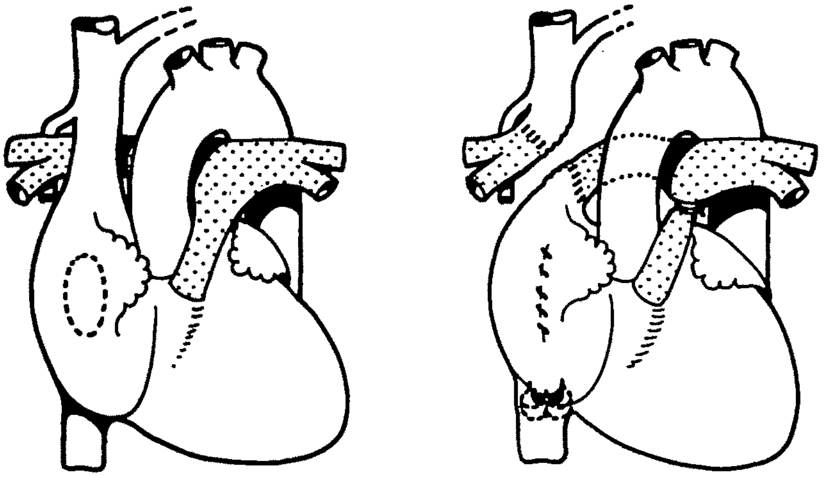

Fig 1. Case 1. Tricuspid atresia type I B. Drawing illustrates the repair: anastomosis between right atrium and proximal end of right pulmonary artery was made without interposition of an aortic valve homograft. (Reproduced from Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8, by permission.)

found normal blood flow through the nonfunctioning right heart could be maintained only under conditions of hypervolemia and marked venous hypertension.

Rodbard and Wagner [14] experimentally bypassed the right ventricle by anastomosis of the right atrial appendage to the main pulmonary artery, demonstrating distal flow when right atrial pressure was sufficiently elevated to 9 to 14 mm saline solution. In staged operations, Warden and associates [15] first produced tricuspid stenosis in dogs and, after a period to allow right atrial hypertrophy and dilatation, subsequently performed a right atrial appendage to pulmonary artery anastomosis. They reported a few survivors and a partial regression in the elevated venous pressure, and suggested future application to the treatment of TA.

Clinically, Hurwitt and associates [16] unsuccessfully attempted right atrial appendage to pulmonary artery anastomosis in a moribund, cyanotic child with univentricular heart. In discussing this report, Schumacker [17] reported three unsuccessful attempts to bypass the right heart for various cyanotic disorders.

The successful results of partial right heart bypass experimentally by Glenn and Patino [5] and Robicsek and co-workers [18] and clinically by Glenn [6] supported the concept of total right heart bypass for TA. From 30% to 40% of total venous return was demonstrated to pass through the superior vena cava–right pulmonary artery [5]. A tendency for chylous pleural effusions postoperatively was noted.

Even though the above experimental and clinical work was completed by 1958, it would still be 10 years before Fontan and Baudet performed the first "physiologic correction." A Fontan-type correction was not even mentioned by Brock [2] in 1964 who, in reporting his unsuccessful ventricular septal defect enlargement procedure conceived a "possible radical cure" for TA in which right atrial–right ventricular continuity would be restored with a prosthetic or homograft valve inserted into the surgically resected area of atretic tricuspid valve.

Fontan and Baudet's general description of surgical technique is a model for a cardiac procedure with multiple steps that minimizes myocardial ischemia. The operation was performed through a median sternotomy. After the anatomy was verified and pulmonary artery pressure and size were measured, a Glenn shunt was performed, delaying superior vena cava ligation until the last step of the procedure to allow subsequent cannulation. Next, with clamps at the base of the right atrial appendage and the origin of the divided right pulmonary artery, an anastomosis between them was made, interposing an aortic homograft. The patient was now placed on cardiopulmonary bypass with a superior vena cava cannula and a right external iliac vein cannula (to allow insertion of the inferior vena cava–right atrial valve), snaring the superior vena cava above the Glenn anastomosis, clamping the inferior vena cava below its junction with the right atrium, venting the left ventricle, and cross-clamping the aorta. Through a right atriotomy, the atrial septal defect was closed and a pulmonary valve homograft inserted into the inferior vena caval orifice. After closure of the atriotomy, the main pulmonary artery was ligated or transected and cardiopulmonary bypass discontinued, maintaining superior vena cava, right atrial, and pulmonary artery pressures "the same or slightly higher" as those measured before bypass. After decannulation, the superior vena cava was transected at its junction with the right atrium and both ends were sutured. With this sequence, the duration of cardiopulmonary bypass was only "about 40 minutes."

Three patients were reported, 2 of whom survived the operation. The first was aged 12 years at the time of Fontan correction. Cardiac catheterization demonstrated a type Ib TA, with pulmonary arteries of good size. Hematocrit preoperatively was 0.80. Operation was performed on April 25, 1968, with measured pulmonary artery pressure of 15/0 mm Hg. The procedure was as described above, except a direct right atrial appendage to pulmonary artery anastomosis was performed because a suitably small valve homograft was not available (Fig 1). Initial postoperative course was smooth, with a blood pressure of 120/60 mm Hg, normal venous pressures, and disappearance of cyanosis. Twenty-four hours postoperatively, anuria developed, corrected with hemodialysis, and melena occurred. The legs were elevated to correct the

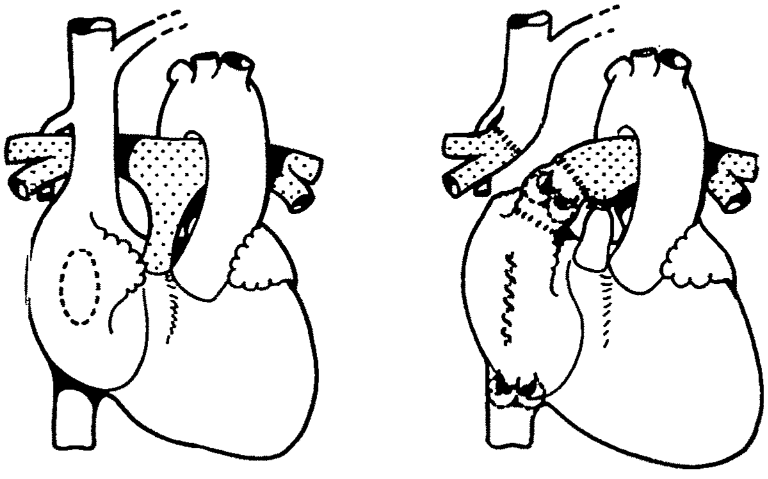

Fig 2. Case 2. Tricuspid atresia type II B. Drawing illustrates steps in surgical repair: (1) end-to-side anastomosis of distal end of right pulmonary artery to superior vena cava; (2) end-to-end anastomosis of right atrial appendage to proximal end of right pulmonary artery by means of an aortic valve homograft; (3) closure of atrial septal defect; (4) insertion of a pulmonary valve homograft into inferior vena cava; and (5) ligation of main pulmonary artery. (Reproduced from Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8, by permission.)

"stagnant inferior vena caval circulation," urine output returned, and a subsequent intravenous pyelogram demonstrated bilateral congenital hydronephrosis. A right pleural effusion required drainage 1 month postoperatively. Fontan and Baudet waited 30 months before their report, at which time the child was growing, had no exercise intolerance, and had a hematocrit of 0.52. A subsequent right atrial angiocardiogram demonstrated no inferior vena cava reflux and excellent forward flow into the left pulmonary artery.

The second patient was 36 years old, with progressive exercise intolerance and cyanosis. Cardiac catheterization demonstrated type IIb TA with nearly normal sized left and right pulmonary arteries. At operation, pulmonary artery pressure was 35/0 mm Hg. The procedure as described above was performed (Fig 2), and although the initial postoperative course was smooth, to maintain adequate blood pressure both hypervolemia and tachycardia with isoproterenol were necessary. A superior vena caval syndrome responded to diuretics, and bilateral serous pleural effusions required drainage. At the time of report, 10 months postoperatively, the patient was doing well with good exercise tolerance and decline of hematocrit from 0.80 to 0.50 with only a "moderate persistent hepatomegaly."

The third patient was operated on at age 23 years and had TA with dextrocardia and low pulmonary artery pressure. Although early postoperative status was reasonable, progressive hypotension occurred in spite of volume replacement and isoproterenol 6 hours postoperatively and the patient died. Autopsy demonstrated patent anastomoses but an abnormal mitral valve with vegetations, and Fontan and Baudet concluded death was due to mitral insufficiency.

In discussing the patients, Fontan and Baudet noted "the striking need to provide a large amount of fluid to ensure a correct hemodynamic balance." The dispensability of the aortic valve homograft was proven by the first patient, although Fontan and Baudet believed its absence contributed to the inferior vena caval syndrome (hepatomegaly, melena, oliguria) seen in that patient. They also emphasized the advantage of low intrapulmonary airway pressures and early extubation, the tendency for pleural effusions requiring diuretic therapy and drainage, and the importance of a normal left ventricle and mitral valve for satisfactory results. They admitted concern about the hemodynamic consequences of subsequent atrial rhythm disturbances such as fibrillation or flutter.

Few new cardiac operations have proved to apply to such various pathology and to allow so many technical modifications as the Fontan procedure. Soon after Fontan and Baudet's report, others reported successful results in TA patients with similar procedures. Kreutzer and associates [19] suggested in 1973 that inferior vena caval valves and Glenn shunts were unnecessary, and used disinsertion of the pulmonic valve with atriopulmonary anastomosis effectively in 2 patients with tricuspid atresia. By 1974, three other groups had survivors with similar procedures using homografts valves [20–22]. An important modification was incorporation of a hypoplastic right ventricle in an effort to augment pulmonary blood flow, as introduced by Bowman and associates [23] and modified by Björk and co-workers [24]. Doty and co-workers [25] emphasized a posterior atriopulmonary connection, less susceptible to sternal compression, and illustrated possible modifications of surgical technique for a wide variety of great artery anatomy. Recently, deLeval and associates [26] described the "cavopulmonary anastomosis" (or "lateral tunnel technique"), which directs inferior vena caval return along the right lateral atrial wall using a patch to the superior vena cava, which is divided and each end sewn end-to-side to the right pulmonary artery. This technique is based on the concept, supported experimentally, that a uniform-sized conduit from inferior vena cava to pulmonary artery has more efficient flow than a larger atrial cavity, which contributes more turbulence. The technique commits the intraatrial defect, tricuspid valve, coronary sinus, and most of the right atrial cavity to the left-sided circulation.

The procedure introduced by Fontan and Baudet became a major breakthrough not only for TA patients but for many with complex, effectively univentricular, hearts. Although septation procedures may be an alternative in a few, the inherent hazards of that procedure make a passive, direct connection between the systemic venous and pulmonary arterial circulation preferable in the great majority when pulmonary artery size and resistance permit [27, 28]. The importance of patient selection remains paramount, with special attention to anatomical variations, timing of operation, pulmonary artery size and resistance, and technical considerations [29, 30]. Patients with mean preoperative pulmonary artery pressure greater than 15 to 20 mm Hg, pulmonary vascular resistance greater than 4 U/m^2, ejection fraction less than 0.45, or ventricular end-diastolic pressures greater than 25 mm Hg are poor candidates for Fontan procedures and should be considered for other palliation [31].

Operative considerations remain very important. Inferior vena caval valves are unnecessary, and prosthetic conduits and heterologous or prosthetic valves should be avoided. Glenn shunts are not mandatory in the majority, but may be advantageous (as end of superior vena cava to side of right pulmonary artery) in select patients [32], and in addition are required with the cavopulmonary technique advocated by deLeval and co-workers [26]. The importance of incorporating a hypoplastic right ventricle or inserting a homograft valve into an atriopulmonary anastomosis remain controversial. Most evidence suggests a hypoplastic right ventricle subsequently provides little, if any, benefit [33–35], and consequently a direct atriopulmonary anastomosis is increasingly favored. As far as the benefit of a homograft valve in this anastomosis, a number of reports suggest a valve in this position provides little benefit and is a source of potential obstruction [35–40]. An atriopulmonary valve may be of benefit, however, in patients with elevated preoperative pulmonary pressures or resistance in the critical early postoperative period to augment pulmonary blood flow. In addition, Fontan and associates [30, 41] have demonstrated better late postoperative exercise capacity when a homograft valve is used.

The importance of atrial contractions, likewise, is controversial, with deLeval and co-workers [26] suggesting that by creating turbulence, contractions may actually impede pulmonary blood flow. The stable condition of patients postoperatively who remain in sinus rhythm conceivably is more a reflection of ventricular function than of the advantage of an atrial contraction per se. Finally, the precepts of postoperative care emphasized in the original report by Fontan and Baudet remain critical.

In approximately 20 years since the first operation, Fontan and Baudet's procedure has taken its place as one of the major advances in congenital heart surgery. By using existing knowledge and extrapolating it to properly selected patients, as well as by meticulous attention to operative and postoperative detail, Fontan and Baudet will forever be remembered for dramatically improving the prognosis of children with TA and other forms of univentricular heart.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8.
2. Brock R. Tricuspid atresia: a step toward corrective treatment. J Thorac Cardiovasc Surg 1964;47:17–25.
3. Taussig HB, Bauersfeld SR. Follow-up studies on the first 1000 patients operated on for pulmonary stenosis or atresia. Ann Intern Med 1953;38:1–8.
4. Sommers SC, Johnson JM. Congenital tricuspid atresia. Am Heart J 1951;41:130–43.
5. Glenn WWL, Patino JF. Circulatory bypass of the right heart. Yale J Biol Med 1954;27:147–51.
6. Glenn WWL. Circulatory bypass of the right side of the heart. IV. Shunt between superior vena cava and distal right pulmonary artery—report of clinical application. N Engl J Med 1958;259:117–20.
7. Starr I, Jeffers WA, Meade RH. The absence of conspicuous increments of venous pressure after severe damage to the right ventricle of the dog, with a discussion of the relation between clinical congestive failure and heart disease. Am Heart J 1943;26:291–301.
8. Bakos ACP. The question of the function of the right ventricular myocardium: an experimental study. Circulation 1950; 1(Pt 2):724–32.
9. Kagan A. Dynamic responses of the right ventricle following extensive damage by cauterization. Circulation 1952;5: 816–23.
10. Donald DE, Essex HE. Pressure studies after inactivation of the major portion of the canine right ventricle. Am J Physiol 1954;176:155–61.
11. Jamison WL, Gemeinhardt W, Alai J, Bailey CP. Artificial maintenance of the systemic circulation without participation of the right ventricle. Circ Res 1954;2:315–8.
12. Rose JC, Broida HP, Hufnagel CA, et al. A method for the study of the circulation using a mechanical left ventricle. J Appl Physiol 1955;7:580–4.
13. Rose JC, Cosimano SJ, Hufnagel CA, et al. The effect of exclusion of the right ventricle from the circulation in dogs. J Clin Invest 1955;34:1625–31.
14. Rodbard S, Wagner D. Bypassing the right ventricle. Proc Soc Exper Biol Med 1949;71:69–70.
15. Warden HE, DeWall RA, Varco RL. Use of the right auricle as a pump for the pulmonary circuit. Surg Forum 1954;5:16–22.
16. Hurwitt ES, Young D, Escher DJW. The rationale of anastomosis of the right auricular appendage to the pulmonary artery in the treatment of tricuspid atresia. J Thorac Surg 1955;30:503–11.
17. Shumacker HB. Discussion of [16]. J Thorac Surg 1955;30:511.
18. Robicsek A, Temesvari A, Kadar RL. A new method for the treatment of congenital heart disease associated with impaired pulmonary circulation. Acta Med Scand 1956;154: 151–61.
19. Kreutzer G, Galindez E, Bono H, et al. An operation for the correction of tricuspid atresia. J Thorac Cardiovasc Surg 1973;66:613–23.
20. Ross DN, Somerville J. Surgical correction of tricuspid atresia. Lancet 1973;1:845–9.
21. Stanford W, Armstrong RG, Cline RE, et al. Right atrium–pulmonary artery allograft for correction of tricuspid atresia. J Thorac Cardiovasc Surg 1973;66:105–11.
22. Miller RA, Pahlajani D, Serratto M, et al. Clinical studies after Fontan's operation for tricuspid atresia [Abstract]. Am J Cardiol 1974;33:157.
23. Bowman FO Jr, Malm JR, Hayes CJ, et al. Physiologic approach to surgery for tricuspid atresia. Circulation 1978; 58(Pt 3):83–6.
24. Björk VO, Olin CL, Bjarke BB, et al. Right atrial–right

ventricular anastomosis for correction of tricuspid atresia. J Thorac Cardiovasc Surg 1979;77:452–8.

25. Doty DB, Marvin WJ Jr, Lauer RM. Modified Fontan procedure: methods to achieve direct anastomosis of the right atrium to pulmonary artery. J Thorac Cardiovasc Surg 1981; 81:470–5.
26. DeLeval MR, Kilner P, Gewilling M, et al. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. J Thorac Cardiovasc Surg 1988;96:682–95.
27. Feldt RH, Mair DD, Danielson GK, et al. Current status of the septation procedure for univentricular heart. J Thorac Cardiovasc Surg 1981;82:93–7.
28. McKay R, Pacifico AD, Blackstone EH, et al. Septation of the univentricular heart with subaortic outlet chamber. J Thorac Cardiovasc Surg 1982;84:77–87.
29. Choussat A, Fontan F, Besse P, et al. Selection criteria for Fontan's procedure. In: Anderson RH, Shinebourne EA, eds. Paediatric cardiology. Edinburgh: Churchill Livingstone, 1977:559–70.
30. Fontan F, Deville C, Quaegebeur J, et al. Repair of tricuspid atresia in 100 patients. J Thorac Cardiovasc Surg 1983;85: 647–60.
31. Haas GS. Laks H, Pearl JP. Modified Fontan procedure. Adv Card Surg 1990;1:111–54.
32. Pennington DG, Nouri S, Ho J, et al. Glenn shunt: long-term results and current role in congenital heart operations. Ann Thorac Surg 1981;31:532–9.
33. Lee CN, Schaff HV, Danielson GK, et al. Comparison of atriopulmonary versus atrioventricular connections for modified Fontan/Kreutzer repair of tricuspid valve atresia. J Thorac Cardiovasc Surg 1986;92:1038–43.
34. Bull C, deLeval MR, Stark J, et al. Use of a subpulmonary ventricular chamber in Fontan circulation. J Thorac Cardiovasc Surg 1983;85:21–31.
35. DiSessa TG, Child JS, Perloff JK, et al. Systemic venous and pulmonary arterial flow patterns after Fontan's procedure for tricuspid atresia or single ventricle. Circulation 1984;70: 898–902.
36. Kreutzer GO, Vargas FJ, Schlicht AJ, et al. Atriopulmonary anastomosis. J Thorac Cardiovasc Surg 1982;83:427–36.
37. Ishikawa T, Neutze JM, Brandt PWT, et al. Hemodynamics following the Kreutzer procedure for tricuspid atresia in patients under 2 years of age. J Thorac Cardiovasc Surg 1984;88:373–9.
38. Shemin RJ, Merrill WH, Pfeifer JS, et al. Evaluation of right atrial pulmonary conduits for tricuspid atresia. J Thorac Cardiovasc Surg 1979;77:685–90.
39. Laks H, Williams WG, Hellenbrand WE, et al. Results of right atrial to right ventricular and right atrial to pulmonary artery conduits for complex congenital heart disease. Ann Surg 1980;192:382–9.
40. Gale AW, Danielson GK, McGoon DC, et al. Modified Fontan operation for univentricular heart and complicated congenital lesions. J Thorac Cardiovasc Surg 1979;78:831–8.
41. Ottenkamp J, Rohmer J, Quaegebeur JM, et al. Nine years' experience with physiologic repair of tricuspid atresia: long term results and current surgical approach. Thorax 1982;37: 718–26.

Supravalvar Aortic Stenosis: A 29-Year Review of Surgical Experience

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Between February 1960 and August 1989, 73 consecutive patients underwent surgical correction for supravalvar aortic stenosis (SVAS) at the Texas Heart Institute. There were 43 male (59%) and 30 female patients (41%) ranging in age from 5 days to 27 years (mean age, 12 years). Preoperatively, 8 patients were in New York Heart Association functional class I, 43 in class II, 18 in class III, and 4 in class IV. Of the 73 patients, 62 had localized SVAS and 11 (15%), diffuse SVAS. For all procedures, patients were placed on cardiopulmonary bypass. Those with localized SVAS were successfully treated with patch aortoplasty, whereas those with diffuse SVAS required either an apicoaortic conduit or extensive endarterectomy with extended patch aortoplasty. There were eight early deaths (≤30 days postoperatively) (11%) and four late deaths (>30 days postoperatively) (6%) in a follow-up period ranging from 2 months to 28 years. Sixteen patients (25%) underwent one or more additional operations in the follow-up period. Postoperatively, there were 44 patients in New York Heart Association functional class I and 17 in class II. Preoperative functional class III and class IV ($p < 0.0005$), diffuse SVAS ($p = 0.05$), and the presence of associated congenital defects ($p < 0.01$) were important determinants of death.

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Supravalvar aortic stenosis (SVAS) is a rare but correctable lesion, which was infrequently diagnosed until the syndrome of "characteristic facies," mental retardation, and SVAS was described by Williams and colleagues [1] in 1961 and Beuren and associates [2] in 1964. Anatomically, three types of SVAS have been described: the hourglass type, the membranous type, and the hypoplastic type [3].

For editorial comment, see page 886.

From the surgical standpoint, SVAS can be divided into two types: a localized form (Fig 1) and a diffuse form (Fig 2). McGoon and co-workers [4] described the surgical approach of using patch aortoplasty in 1961, and this has remained the standard corrective procedure for localized SVAS; however, the treatment of diffuse SVAS continues to pose a serious challenge. We describe postoperative results in 73 consecutive patients who underwent surgical correction for SVAS at the Texas Heart Institute during a 29-year period.

Material and Methods

Patient Population

Of the 73 patients who underwent surgical correction for SVAS between February 1960 and August 1989, 43 (59%) were male and 30 (41%) were female. The age range was 5 days to 27 years (mean age, 12 years). For the purpose of review, we divided our patients into four groups based on the diagnosis of SVAS and associated lesions (Table 1).

Sixteen patients (22%) had undergone previous operations, which included repair of coarctation of the aorta (4), Dacron patch aortoplasty and aortic valvotomy (3), aortic valvotomy (3), resection of subaortic stenosis (1), repair of aortic arch interruption (1), pulmonary valvotomy (1), ligation of persistent ductus arteriosus (1), ligation of persistent ductus arteriosus and aortic valvotomy (1), and ligation of persistent ductus arteriosus and pulmonary artery banding (1). A definite family history was present in 2 patients whose fathers had had congenital valvar aortic stenosis and in 1 patient whose siblings had SVAS. Other associated factors included features of Williams syndrome in 14 patients, rubella syndrome in 5 patients, and mental retardation in 3. Five patients were Jehovah's Witnesses.

Thirty-three patients (45%) were admitted with a history of heart murmur. Syncope (13 patients, 18%), easy fatigability (13 patients), dyspnea on exertion (9 patients, 12%), and chest pain (9 patients) were the common symptoms. The chest roentgenogram was normal in 51 patients (70%) and revealed mild to moderate cardiomegaly in 22 patients (30%). The electrocardiogram was normal in 26 patients (36%) and showed left ventricular hypertrophy, with or without strain, in 34 patients (47%), biventricular hypertrophy in 7 (9%), right bundle-branch block in 4 (5%), and ventricular arrhythmias in 2 (3%). Cardiac catheterization and angiography were performed in 65 patients, and hemodynamic studies had been done at other institutions in an additional 5 patients. Three

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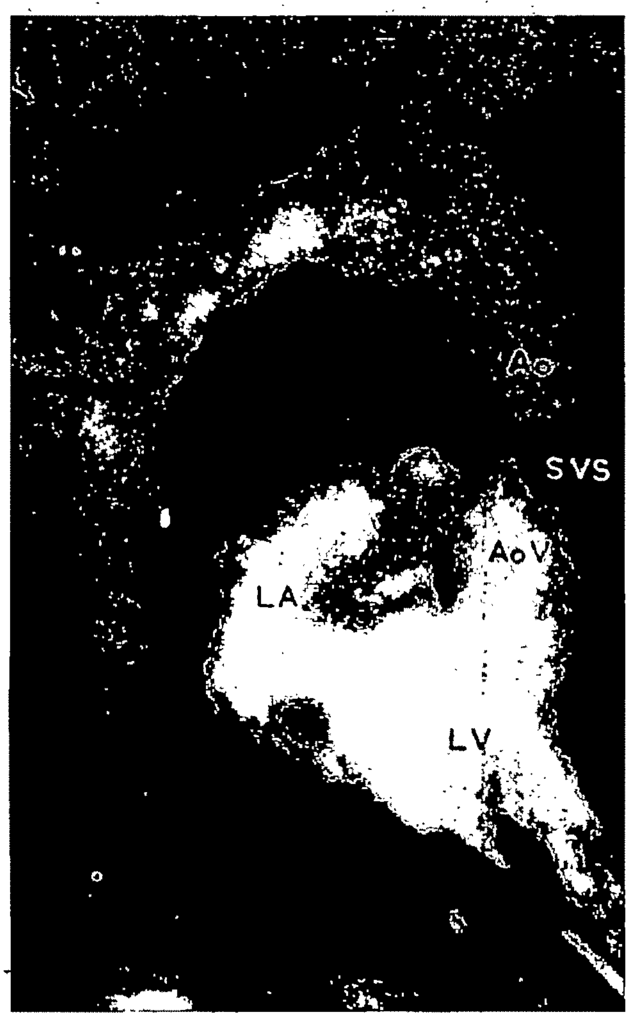

Fig 1. Preoperative angiogram showing localized form of supravalvar aortic stenosis. (Ao = *aorta;* AoV = *aortic valve;* LA = *left atrium;* LV = *left ventricle;* SVS = *supravalvar stenosis.)*

Table 1. Patient Groups by Diagnosis

Group	No. of Patients	
1: Patients with isolated, localized SVAS	24	
2: Patients with localized SVAS and associated obstructive lesions of LVOT	33	
SVAS and valvar aortic stenosis		22
SVAS and subaortic stenosis[a]		4
SVAS and valvar and subaortic stenosis		7
3: Patients with diffuse SVAS	11	
Without associated cardiac defects		5
With associated cardiac defects		6
4: Patients with SVAS complicated by associated congenital cardiac defects, infective endocarditis	5	
SVAS with mycotic aneurysm of ascending aorta		1
SVAS with pseudoaneurysm of ascending aorta		1
SVAS with VSD, subaortic stenosis, and banding of pulmonary artery		1
SVAS with obstructed PAPVR (left lung) to left SVC draining into left atrium, bidirectional PDA, mild mitral regurgitation, severe aortic stenosis, and endocardial fibroelastosis		1
SVAS with severe stenosis of main and branch pulmonary arteries		1

[a] This includes discrete, diffuse, or "tunnel" subaortic stenosis.

LVOT = left ventricular outflow tract; PAPVR = partial anomalous pulmonary venous return; PDA = persistent ductus arteriosus; SVAS = supravalvar aortic stenosis; SVC = superior vena cava; VSD = ventricular septal defect.

patients underwent operation without having invasive diagnostic procedures.

The left ventricular systolic pressure ranged between 130 and 300 mm Hg (mean pressure, 190 mm Hg), and the

Fig 2. Preoperative angiogram showing diffuse form of supravalvar aortic stenosis and postendarterectomy specimen from patient with this form.

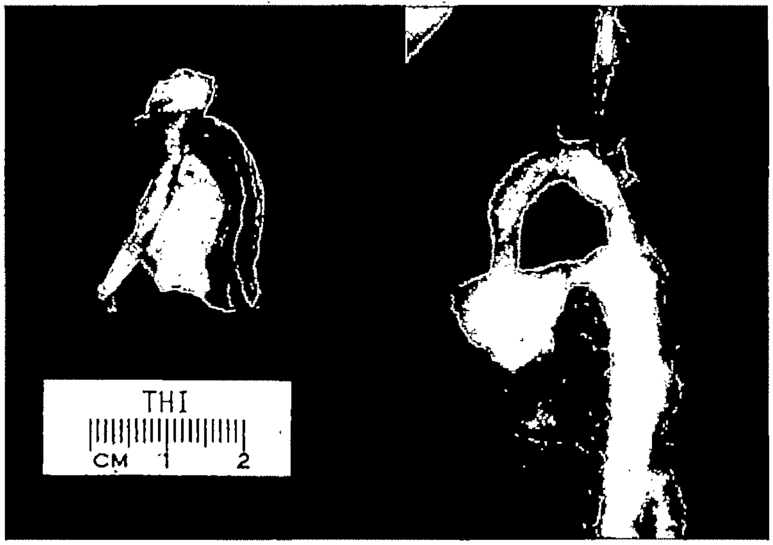

Table 2. Operative Procedures

Procedures	No. of Patients	
Group 1	24	
DPA		24
Group 2	33	
DPA and aortic valvotomy		14
DPA and AVR		7
DPA, aortic valvotomy, and subvalvar resection		5
DPA and subvalvar resection		4
DPA, AVR, and subvalvar resection		2
DPA, AVR, and ligation of PDA		1
Group 3	11	
DPA and aortic valvotomy		1
Apicoaortic conduit		6
Apicoaortic conduit (with 7-mm Dacron tube graft bypass from left subclavian to left common carotid and innominate arteries)		1
Extensive endarterectomy of ascending aorta and arch vessels with DPA		2
Extensive endarterectomy of arch vessels with interposition graft replacement of ascending aorta and arch		1
Group 4	5	
Pericardial patch aortoplasty with repair of mycotic aneurysm of ascending aorta		1
Repair of pseudoaneurysm of ascending aorta with 16-mm interposition graft, ligation of PDA, and resuspension of aortic valve		1
Debanding of pulmonary artery, closure of VSD, subaortic resection with patch aortoplasty		1
DPA, ligation of PDA, aortic valvotomy, and subaortic resection		1
DPA with Hegar's dilation of main and branch pulmonary arteries		1

AVR = aortic valve replacement; DPA = Dacron patch aortoplasty; PDA = persistent ductus arteriosus; VSD = ventricular septal defect.

pressure gradient across the left ventricular outflow tract ranged between 80 and 180 mm Hg (mean range, 88 mm Hg). Preoperatively, 8 patients were in New York Heart Association functional class I, 43 were in class II, 18 were in class III, and 4 were in class IV.

Operative Techniques

The details of the procedures performed are provided in Table 2, and illustrations of operative techniques are shown in Figure 3. All procedures were done with the use of cardiopulmonary bypass, with or without hypothermia. The patch aortoplasty and apicoaortic conduit techniques have been reviewed previously by Cooley and colleagues [5, 6].

Total circulatory arrest was used in 3 patients with diffuse SVAS. Standard cardiopulmonary bypass was established, and the patient was cooled to a core temperature of 18°C. The circulation was stopped, and a longitudinal incision was made over the ascending aorta and extended into the noncoronary cusp proximally and to the transverse arch distally. An extensive endarterectomy of the ascending aorta and the arch vessels was performed in 2 patients (Fig 4). The ascending aorta was excised in an adult patient. The repair was completed with a woven Dacron patch in 2 patients and with an 18-mm interposition Dacron tube graft in the third patient. The circulation was reinstituted, and the patient was rewarmed to 37°C and weaned from cardiopulmonary bypass. Only 1 patient had major stenosis of the main and branch pulmonary arteries requiring intraoperative dilation with a Hegar's dilator. Before 1977, only ischemic arrest with intermittent cross-clamping of the aorta was employed for myocardial protection. Since then, cold hyperkalemic crystalloid solution has routinely been used.

All the patients in group 1 and group 2 underwent Dacron patch aortoplasty: a diamond-shaped patch was used in 50 patients, and a modified Dacron patch was used in 7 patients. Group 2 patients also underwent operation for associated lesions. In the first patient in group 3, an attempt to repair the diffuse form of SVAS with patch aortoplasty was unsuccessful in abolishing the pressure gradients; therefore, an apicoaortic conduit was used in the next 7 patients in accordance with the technique described by Cooley and associates [6]. The last 3 patients in this group underwent extensive endarterectomy of the ascending aorta and arch vessels under total circulatory arrest. In 1 adult patient in the group, the ascending aorta was replaced with an 18-mm interposition graft of Dacron. Operative procedures were individualized for the 5 patients in group 4.

Results

Of the 73 patients, 65 survived and have been followed up for a period ranging from 2 months to 28 years. Information regarding these patients was obtained from their charts and from the referring physicians. Sixteen patients required an additional operation during follow-up (Table 3).

The study period was divided into three decades, and these decades were compared with reference to the number of patients undergoing procedures and the postoperative outcome. Among the 12 patients who had operation from 1960 through 1969, there were three early deaths. Among the 36 patients who had operation from 1970 through 1979, there were five early deaths and four late deaths. Among the 25 patients who had operation from 1980 to 1989, there were no early or late deaths.

Early Deaths and Complications

In the total group, there were eight early deaths (11%). Information regarding procedures and causes of death is outlined in Table 4. Among the 24 patients in group 1, there was one early death. The patient died on the first postoperative day after experiencing seizures. Postmortem examination revealed a subdural hematoma with herniation of the brain and an incidental reticular cell sarcoma.

Of the 33 patients in group 2, 4 died in the early

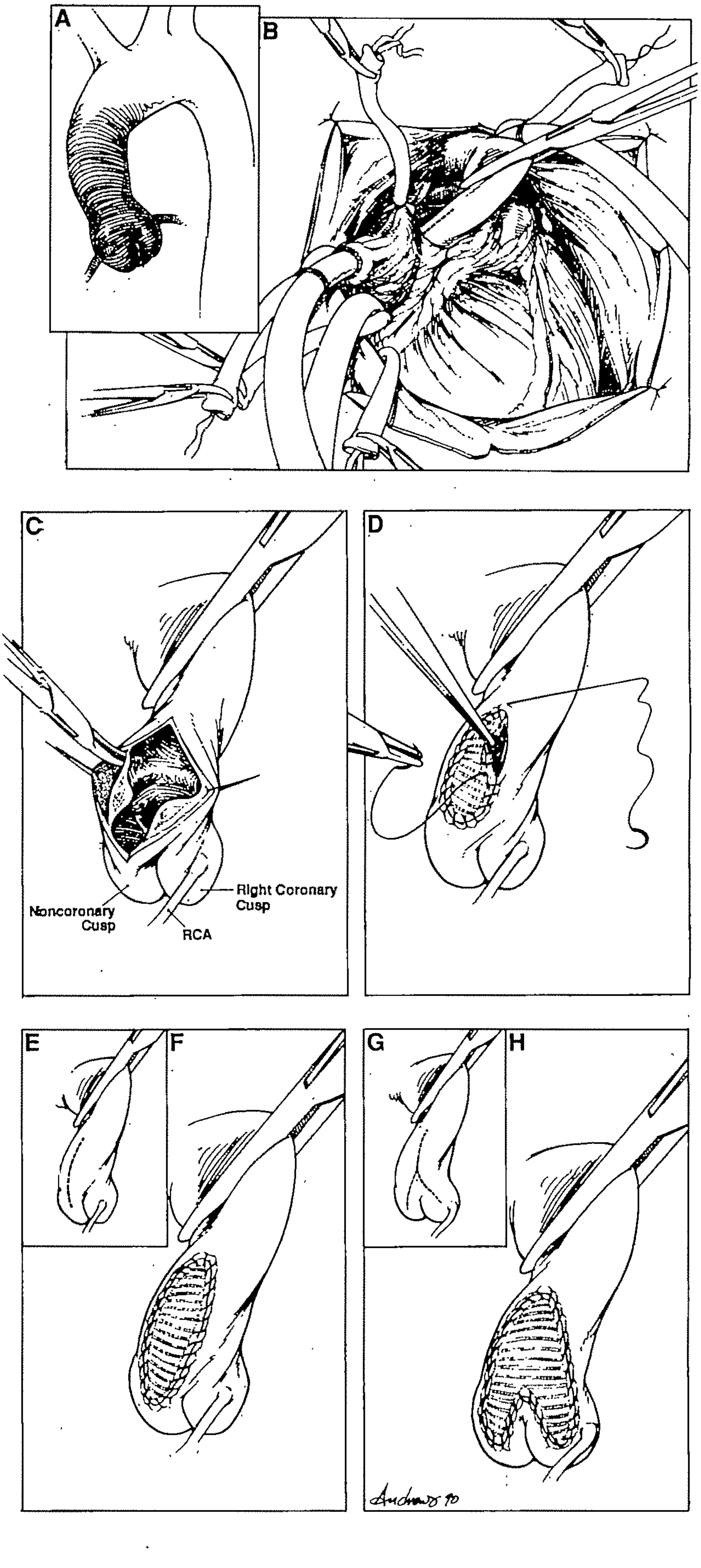

Fig 3. (A) External appearance of supravalvar aortic stenosis. (B) Standard cardiopulmonary bypass technique. (C) Endarterectomy procedure. (D) Pericardial patch repair. (E, F) Standard patch aortoplasty. (G, H) Extended patch aortoplasty. (RCA = right coronary artery.)

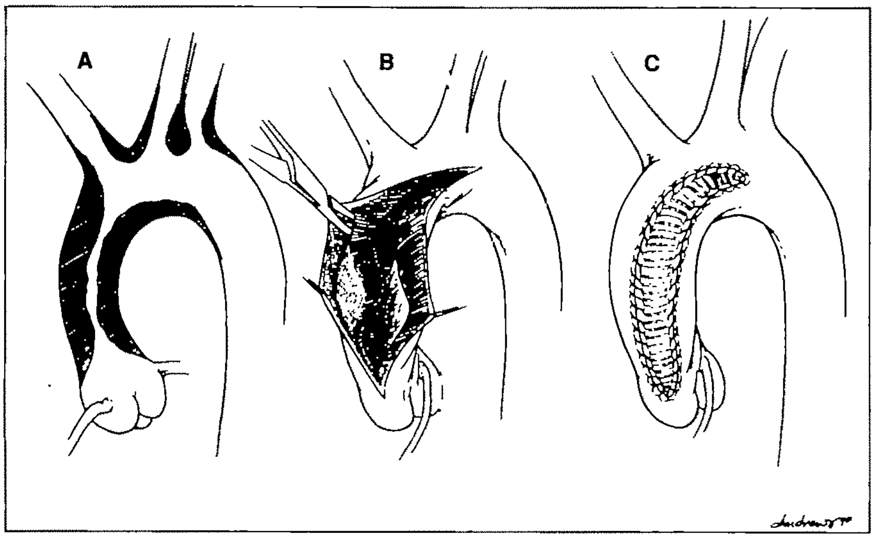

Fig 4. Technique of extensive endarterectomy for diffuse supravalvar aortic stenosis.

postoperative period. The causes of death in 2 of them was ventricular arrhythmias. Another patient, who was a Jehovah's Witness, experienced right coronary artery injury and anemia in the postoperative period, both of which contributed to ventricular arrhythmias and death. The fourth patient, a high-risk 5-day-old neonate, underwent emergent aortic valvotomy with patch aortoplasty. He died 20 hours after the procedure of acute left ventricular failure associated with acute aortic regurgitation.

The only death among group 3 patients occurred in a Jehovah's Witness who underwent apicoaortic conduit replacement after a previous unsuccessful Dacron patch aortoplasty. He died of postoperative bleeding.

Two of the 5 patients in group 4 died early. The first was a 2-week-old neonate with multiple lesions who could not be weaned from cardiopulmonary bypass, and the second was a Jehovah's Witness with severe stenosis of the main and branch pulmonary arteries who died of postoperative bleeding. Branch pulmonary artery stenosis, although present in 16% of our patients, was not critical enough to require surgical treatment in any patient except 1 and did not contribute to any pulmonary complications in the postoperative period.

Table 3. Operations Performed During Follow-up

Operation	No. of Patients
Aortic valve replacement[a]	3
Redo aortic valve replacement	2
Apicoaortic conduit	2
Replacement of apicoaortic conduit	2
Modified Konno procedure for residual subaortic stenosis	2[b]
Removal of infected conduit with aortic valvotomy and Dacron patch aortoplasty	1
Aortic valvotomy followed 2 years later by aortic valve replacement	1
Closure of residual left ventricular–right atrial left-to-right shunt	1
Redo repair of coarctation	1
Redo repair of aortic arch interruption	1

[a] Aortic valve replacement was done for aortic regurgitation after previous aortic valvotomy. [b] These 2 patients had "tunnel" subaortic stenosis, which in both was incompletely relieved during the first procedure.

Early nonfatal complications included surgical exploration for bleeding in 5 patients, transient supraventricular arrhythmias in 3 patients, signs of postpericardiotomy syndrome in 5 patients, and mild wound infections in 2 patients.

Late Deaths and Complications

There were four late deaths, all of which were attributed to infective endocarditis. Three of the 4 patients had undergone an apicoaortic conduit procedure to relieve the symptoms. The fourth patient had a pseudoaneurysm of the ascending aorta with aortic regurgitation, which necessitated resuspension of the aortic valve and replacement of the ascending aorta with a 16-mm interposition conduit. All these patients underwent multiple procedures before finally dying of severe infection. The operations and causes of death are described in Table 5.

The nonfatal late complications included residual valvar aortic stenosis in 3 patients, mild stenosis and regurgitation in 1 patient, and mild mitral regurgitation in 1 patient.

Functional Class

Postoperatively, there were 44 patients in New York Heart Association class I and 17 patients in class II. The change from preoperative functional status to postoperative status is shown in Figure 5. All 4 patients in class IV died, as did 5 of the 18 patients in class III.

Statistical Analysis

We performed χ^2 tests to determine the association of death (early and late) with various factors. Preoperative

Table 4. Early Deaths

Year	Age	Sex	NYHA Class	Diagnosis	Procedures	Death	
						Time Postop	Cause
Group 1							
1976	11 y	M	III	SVAS	DPA	1 d	Seizures, low cardiac output[a]
Group 2							
1960	6 y	F	III	SVAS, valvar AS	DPA, aortic valvotomy	4 h	Ventricular arrhythmia[b]
1968	22 y (JW)	F	II	SVAS, subvalvar AS	DPA, subaortic resection	8 d	Ventricular arrhythmia
1968	6 y	M	II	SVAS, subvalvar AS	DPA, subaortic resection	5 h	Ventricular arrhythmia
1972	5 d	M	IV	SVAS, AS	DPA, aortic valvotomy	20 h	Acute LV failure (acute AR)[c]
Group 3							
1977	9 y (JW)	M	II	SVAS, subvalvar AS (s/p subaortic resection and aortic valvotomy)	Apicoaortic conduit (redo)	10 h	Bleeding
Group 4							
1975	14 d	M	IV	SVAS, PAPVR, PDA, LSVC, MR, severe AS, endocardial fibroelastosis	Ligation of PDA, subaortic resection, aortic valvotomy, DPA	Could not be weaned from CPB[d]	
1977	8 y (JW)	F	III	SVAS, severe stenosis of main and branch pulmonary arteries	DPA, dilation of main and branch pulmonary arteries	12 h	Bleeding

[a] Autopsy revealed a subdural hematoma with herniation of the brain and reticular cell sarcoma. [b] Autopsy revealed a rheumatic lesion of the mitral and aortic valves. [c] Arrest occurred before catheterization. [d] Arrest occurred before the patient could be weaned from CPB.

AR = aortic regurgitation; AS = aortic stenosis; CPB = cardiopulmonary bypass; DPA = Dacron patch aortoplasty; JW = Jehovah's Witness; LSVC = left superior vena cava; LV = left ventricular; MR = mitral regurgitation; NYHA = New York Heart Association; PAPVR = partial anomalous pulmonary venous return; PDA = persistent ductus arteriosus; s/p = status post; SVAS = supravalvar aortic stenosis.

New York Heart Association functional class III and class IV ($p < 0.0005$), diffuse SVAS ($p = 0.05$), and the presence of associated congenital defects ($p < 0.01$) were important determinants of operative death.

Comment

Supravalvar aortic stenosis has been known to occur in three forms: familial, sporadic, and in association with peculiar facies. Among the etiological factors implicated are idiopathic hypercalcemia, disturbance of vitamin D and calcium homeostasis, and rubella [7–10]. The high incidence of associated cardiac anomalies, including abnormalities of the aortic valve, coronary arteries, aortic arch vessels, pulmonary valve, pulmonary arteries, and mitral valve, has been described [3, 11, 12]. These anomalies were all seen in our patient population (Table 6).

The approach of McGoon and associates [4], ie, using patch aortoplasty, remains the standard operative procedure for localized SVAS. Other procedures to correct SVAS include manual dilation of the stenotic area [13], partial excision of the stenotic area [14], and excision and end-to-end anastomosis of the ascending aorta [15]. Gordon [16] performed the first successful operation for SVAS with the use of moderate hypothermia. An aortoplasty procedure with a diamond-shaped patch placed across the stenotic area and extending into the noncoronary sinus is successful in many patients with SVAS, but it is inadequate in patients with more severe cases, especially the diffuse form [17–21]. The aortoplasty technique was modified by Doty and co-workers [22] by incising the supravalvar ring at two points in the noncoronary and the right coronary sinus of Valsalva. The repair was achieved with an inverted V-shaped Dacron patch to provide a wide aortic cross-sectional area. This extended aortoplasty resulted in complete relief for patients with localized SVAS [22, 23].

The initial operative mortality associated with surgical repair for diffuse SVAS was 50% to 60% [17, 19, 24]. The diffuse type of lesion was considered to be inoperable because those patients who did survive after patch aortoplasty continued to have persistent gradients across the left ventricular outflow tract [17, 19]. An alternative way to treat this lesion was described by Cooley and associates [6] in 1975. They [24–26] have used an apicoaortic conduit to provide complete relief of left ventricular hypertension and achieve a low mortality in patients with diffuse SVAS. Merin and colleagues [27] reported successful repair of diffuse SVAS in 1 patient. They described an extended

Table 5. Late Deaths

Date of Admission	Age (y)	Sex	NYHA Class	Diagnosis	Procedures	Cause of Death
Group 3: Patient 1						
Sep 1977	12	M	III	Diffuse SVAS with valvar AS (s/p ligation of PDA and aortic valvotomy)	Apicoaortic conduit with 16-mm PV conduit	. . .
Dec 1977	. . .	. . .	. . .	Severe infective endocarditis	Removal of conduit, aortic valvotomy, and DPA	. . .
Jan 1978	. . .	. . .	. . .	. . .	. . .	Secondary hemorrhage from left ventricular apex
Group 3: Patient 2						
April 1973	5	M	IV	Diffuse SVAS and valvar AS (rubella)	DPA and aortic valvotomy	. . .
Oct 1975	7	. . .	. . .	Residual gradient across LVOT	Apicoaortic conduit with 14-mm PV conduit	. . .
Dec 1979	11	. . .	. . .	AR with porcine valve dysfunction	AVR with 19-mm IS valve and replacement of conduit valve with 16-mm PV	. . .
April 1980	12	. . .	. . .	Infective endocarditis	Medical treatment	. . .
May 1980	. . .	. . .	. . .	. . .	. . .	Massive GI bleeding; autopsy: pseudoaneurysm of ascending aorta with rupture into esophagus
Group 3: Patient 3						
Dec 1976	15 (JW)	F	IV	Diffuse SVAS with stenosis of arch vessels	Apicoaortic conduit with 18-mm PV conduit	. . .
Jan 1977	. . .	. . .	. . .	Stenosis of arch vessels	Bypass graft from LSA to LCC and innominate artery	. . .
Feb 1980	19	. . .	. . .	Infective endocarditis	Medical treatment	. . .
March 1982	21	. . .	. . .	Porcine valve dysfunction	Replacement of conduit valve with 18-mm PV	Septicemia
Group 4: Patient 4						
Nov 1972	7	F	III	SVAS with AR, PDA, and pseudoaneurysm of ascending aorta (s/p infective endocarditis)	Ligation of PDA, repair AV with 16-mm interposition graft to replace ascending aorta	. . .
April 1973	8	. . .	. . .	AR	AVR with 17-mm BS valve	. . .
Dec 1973	. . .	. . .	. . .	Periprosthetic valvar leak	DPA	. . .
Jan 1975	9	. . .	. . .	. . .	. . .	Died at home (cause?)

AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve; AVR = aortic valve replacement; BS = Björk-Shiley; DPA = Dacron patch aortoplasty; GI = gastrointestinal; IS = Ionescu-Shiley; JW = Jehovah's Witness; LCC = left common carotid artery; LSA = left subclavian artery; LVOT = left ventricular outflow tract; NYHA = New York Heart Association; PDA = persistent ductus arteriosus; PV = pulmonary valve; s/p = status post; SVAS = supravalvar aortic stenosis.

aortoplasty with application of a large pericardial patch to enlarge the ascending aorta and the origin of the innominate artery with a 6-mm Dacron tube bypass graft from the ascending aorta to the left common carotid artery. Doty and co-authors [22] recommended extended aortoplasty as the initial procedure in patients with diffuse SVAS. Thevenet [28] successfully treated a patient with diffuse SVAS by an extended aortic endarterectomy and

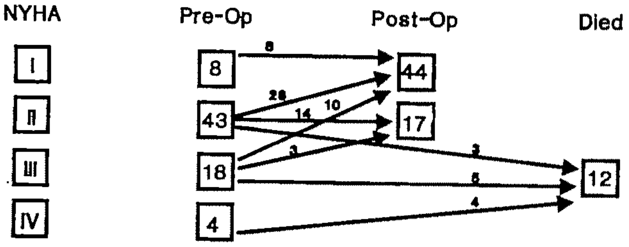

Fig 5. Correlation of surgical outcome with New York Heart Association (NYHA) functional status. The postoperative follow-up ranged from 2 months to 28 years.

symmetrical enlargement of the supravalvar ring in all three sinuses of Valsalva.

In our series, 11 patients had diffuse SVAS (group 3). A standard patch aortoplasty was unsuccessful in the first patient. The next 7 patients, most of whom had previously undergone unsuccessful operations, were successfully treated with an apicoaortic conduit. (The first patient also had had an apicoaortic bypass to relieve the pressure gradients.) The remaining 3 patients underwent extensive endarterectomy of the ascending aorta, aortic arch, and arch vessels with an extended Dacron patch aortoplasty; these procedures were done with the use of profound hypothermia and total circulatory arrest. In 1 of the 3 patients, an 18-mm interposition Dacron graft partially replaced the ascending aorta.

Currently, we perform an extended endarterectomy of the ascending aorta and the arch vessels, followed by a Dacron patch repair to relieve diffuse SVAS. The repair can also be accomplished with an interposition Dacron graft after excision of part of a severely diseased ascending aorta in adult patients with this condition. Use of apicoaortic conduits helps to relieve pressure gradients but does nothing to prevent the actual or potential obstruction of the coronary arteries [22]. In addition, associated complications, including infective endocarditis, conduit stenosis, and porcine valve dysfunction, have made this approach less favorable. In our opinion, this procedure should be reserved only for difficult cases in which previous attempts to relieve pressure gradients have been unsuccessful.

Table 6. Associated Cardiovascular Lesions

Lesion	No. of Patients	Percent
Bicuspid aortic valve	18	25
Branch pulmonary artery stenosis	12	16
Aortic regurgitation	9	12
Aortic stenosis (valvar)	8	11
Aortic stenosis (subvalvar)	7	10
Enlargement of sinus of Valsalva with dilation of coronary arteries	8	11
Ventricular septal defect	3	4
Mitral regurgitation	3	4
Coarctation of aorta	4	6
Persistent ductus arteriosus	2	3
Stenosis of arch vessels	2	3
Mycotic aneurysm of ascending aorta	1	1
Systemic venous abnormalities	1	1

Three of the patients who died early were Jehovah's Witnesses, and they died of postoperative bleeding complications. In these patients, transfusions of blood or blood products could not be used, and this might have altered the outcome. One of these patients also had an inadvertent injury to the right coronary artery, which might have contributed to her death. Ventricular arrhythmias, which caused death in an additional 3 patients, may have resulted from inadequate myocardial protection in hypertrophied left ventricles compounded by a sudden decrease in proximal coronary artery hypertension.

All the early deaths occurred when we were using ischemic arrest with intermittent cross-clamping of the ascending aorta. Since we began routine use of cold hyperkalemic crystalloid cardioplegic solution in 1977, 43 patients have undergone SVAS procedures without any early deaths. Use of cardioplegia provides optimal myocardial protection with a completely relaxed heart in a bloodless field; this may have contributed to the low incidence of postoperative arrhythmias and bleeding since 1977. All the late deaths in our patients were attributed to infective endocarditis.

In conclusion, a good surgical outcome can be achieved with the appropriate method of treatment in patients with both localized and diffuse SVAS.

References

1. Williams JCP, Barratt-Boyes BG, Lowe JB. Supravalvular aortic stenosis. Circulation 1961;24:1311–8.
2. Beuren AJ, Schulze C, Eberle P, Harmjanz D, Apitz J. The syndrome of supravalvular aortic stenosis, peripheral pulmonary stenosis, mental retardation and similar facial appearance. Am J Cardiol 1964;13:471–83.
3. Peterson TA, Todd DB, Edwards JE. Supravalvular aortic stenosis. J Thorac Cardiovasc Surg 1965;50:734–41.
4. McGoon DC, Mankin HT, Vlad P, Kirklin JW. The surgical treatment of supravalvular aortic stenosis. J Thorac Cardiovasc Surg 1961;41:125–33.
5. Hallman GL, Cooley DA. Surgical treatment of congenital heart disease. 3rd ed. Philadelphia: Lea & Febiger, 1987:72–3.
6. Cooley DA, Norman JC, Mullins CE, Randall C. Left ventricle to abdominal aortic conduit for relief of aortic stenosis. Cardiovasc Dis (Bull Tex Heart Inst) 1975;2:376–83.
7. Garcia RE, Friedman WF, Kaback MM, Rowe RA. Idiopathic hypercalcemia and supravalvular aortic stenosis: documentation of a new syndrome. N Engl J Med 1964;271:117.
8. Martin EC, Moseley IF. Supravalvar aortic stenosis. Br Heart J 1973;35:758–65.
9. Varghese PJ, Izukawa T, Rowe RD. Supravalvular aortic stenosis as part of rubella syndrome, with discussion of pathogenesis. Br Heart J 1969;31:59–62.
10. Antia AU, Wiltse HE, Rowe RD, et al. Pathogenesis of the supravalvular aortic stenosis syndrome. J Pediatr 1967;71: 431–41.
11. Neufeld HN, Wagenvoort CA, Ongley PA, Edwards JE. Hypoplasia of ascending aorta: an unusual form of supraval-

vular aortic stenosis with special reference to localized coronary arterial hypertension. Am J Cardiol 1962;10:746–51.

12. Becker AE, Becker MJ, Edwards JE. Mitral valvular abnormalities associated with supravalvular aortic stenosis: observations in 3 cases. Am J Cardiol 1972;29:90–4.
13. Kreel I, Reiss R, Strauss L, Blumenthall S, Baronofsky ID. Supravalvular stenosis of the aorta. Ann Surg 1959;149: 519–24.
14. Hancock E. Differentiation of valvular, subvalvular and supravalvular aortic stenosis. Guy's Hosp Rep 1961;110:1–30.
15. Hara M, Dungan T, Lincoln B. Supravalvular aortic stenosis: report of successful excision and aortic re-anastomosis. J Thorac Cardiovasc Surg 1962;43:212–21.
16. Gordon AS. The surgical management of congenital supravalvular, valvular, and subvalvular aortic stenosis using deep hypothermia. J Thorac Cardiovasc Surg 1962;43:141–56.
17. Rastelli GC, McGoon DC, Ongley PA, Mankin HT, Kirklin JW. Surgical treatment of supravalvular aortic stenosis: report of 16 cases and review of literature. J Thorac Cardiovasc Surg 1966;51:873–82.
18. Pansegrau DG, Kioshos JM, Durnin RE, Kroetz FW. Supravalvular aortic stenosis in adults. Am J Cardiol 1973;31: 635–40.
19. Bernhard WF, Keane JF, Fellows KE, Litwin SB, Gross RE. Progress and problems in the surgical management of congenital aortic stenosis. J Thorac Cardiovasc Surg 1973;66: 404–19.
20. Weisz D, Hartmann AF, Weldon CS. Results of surgery for congenital supravalvular aortic stenosis. Am J Cardiol 1976; 37:73–7.
21. Flaker G, Teske D, Kilman J, Hosier D, Wooley C. Supravalvular aortic stenosis: a 20-year clinical perspective and experience with patch aortoplasty. Am J Cardiol 1983;51:256–60.
22. Doty DB, Polansky DB, Jenson CB. Supravalvular aortic stenosis: repair by extended aortoplasty. J Thorac Cardiovasc Surg 1977;74:362–71.
23. Stewart S, Alexson C, Manning J. Extended aortoplasty to relieve supravalvular aortic stenosis. Ann Thorac Surg 1988; 46:427–9.
24. Keane JF, Fellows KE, LaFarge CG, Nadas AS, Bernhard WF. The surgical management of discrete and diffuse supravalvar aortic stenosis. Circulation 1976;54:112–7.
25. Cooley DA, Norman JC, Reul GJ Jr, Kidd JN, Nihill MR. Surgical treatment of left ventricular outflow tract obstruction with apicoaortic valved conduit. Surgery 1976;80:674–80.
26. Sweeney MS, Walker WE, Cooley DA, Reul GJ. Apicoaortic conduits for complex left ventricular outflow obstruction: 10-year experience. Ann Thorac Surg 1986;42:609–11.
27. Merin G, Copperman IJ, Borman JB. Surgical correction of diffuse supravalvular aortic stenosis involving the branches of the aortic arch. Chest 1976;70:546–9.
28. Thevenet A. Symmetric enlargement of the ascending aorta in supravalvular aortic stenosis of the diffuse type: an alternative to apico-aortic conduit. J Cardiovasc Surg (Torino) 1981;22:1–8.

Notes From the Thoracic Surgery Directors Association

The Thoracic Surgery Directors Association (TSDA) met in San Francisco, CA, on February 16, 1991.

Dr William A. Gay, Jr, announced the establishment of the Thoracic Surgery Directors Association Resident Award for the best scientific abstract at the annual meeting of The Society of Thoracic Surgeons. The award was founded by the TSDA with sponsorship by Medtronic, Inc, to encourage excellence in cardiovascular research. Dr Todd L. Demmy was introduced as the first recipient of the TSDA Resident Award for his abstract "Resuscitation of Injured Myocardium with Adenosine and Biventricular Assist." Dr Demmy, whose program director is George J. Magovern, MD, is a senior thoracic resident in the Department of Surgery at Allegheny General Hospital in Pittsburgh, PA. This distinguished award was presented to Dr Demmy by Dr Glen D. Nelson, Vice-Chairman, Medtronic, Inc, who emphasized his interest in encouraging the academic process and that the award would be annual. Dr Magovern and Dr Demmy both reflected on the value of a research experience in thoracic residency training during their remarks of appreciation.

Harvey W. Bender, Jr, MD, reported from the American Board of Thoracic Surgery. Dr Bender reported that Dr W. Gerald Austen has completed his term on the American Board of Thoracic Surgery and his position will be filled by Mortimer J. Buckley, MD. Written examination results from the Board will be available early in the spring. Dr Bender encouraged the support of the TSDA in the recertification process. He emphasized that the process was a valuable self-teaching/learning procedure. In reference to credentialing, Dr Bender stressed that program directors should be evaluators and not advocates of resident candidates. Criteria for operative case credit must be looked at very carefully, and the trainee must be kept involved in all aspects of the patient's care. Coordination with the Residency Review Committee (RRC) may be required to solve the problem of inadequately prepared trainees.

John L. Ochsner, MD, reported from the RRC for Thoracic Surgery. He expanded on Dr Bender's comment relating to the inadequately prepared trainee and suggested that the RRC would be responsive to efforts to provide a candidate 6 or more months of additional training if the effort does not compromise other residents in the program. The RRC met recently and reviewed 23 programs. The RRC reaffirmed the 125 case per year guideline for operative experience and will continue the present policy for length of training. The RRC has taken a strong position in favor of participation by program directors in the TSDA match. The RRC does not endorse the setting of specific limits on working hours and call schedules as presented by the Accreditation Council for Graduate Medical Education. Dr Ochsner assured the membership that the RRC will be appropriately represented when the RRC for general surgery reviews vascular surgery programs. In closing, Dr Ochsner expressed concern for those who have received emergency call to the military service related to the Persian Gulf crisis and assured the membership that the RRC will do its best to provide sympathetic consideration.

Representing the RRC for Surgery, Paul Friedmann, MD, provided the RRC Policy Statement on Working Environment dated January 8, 1991:

> Postgraduate surgical training differs from that of many other specialties in medicine. The nature of surgical disease and the unique relationship of the surgeon with a patient make continuity of care and the responsibility for that continuity essential elements of surgical education. Decisions about surgical intervention must be based on careful continuing reevaluation of the patient by the same surgical team. The outcome of surgical therapy is critically dependent upon choosing the proper treatment at the proper time. Delays and miscommunication can mean the difference between a good outcome and poor outcome, or between life and death. Surgeons must learn that responsibility for continuity of care is of the highest priority. This sense of responsibility cannot be properly developed in an environment in which the frequency of night call or the number of hours worked per week are primary considerations. . .
>
> The Residency Review Committee for Surgery has explicitly stated in the revised Special Requirements that the working environment for surgical residents must be structured so that undue stress and fatigue are avoided. Appropriate supervision must be provided. Residents should not be required to perform excessively difficult or prolonged duties regularly. The provision of adequate support services and systems so that residents are not required to be engaged in activities extraneous to their educational goals is also essential. In this overall context, however, the RRC believes very strongly that the requirements for continuing responsibility of care must be the overriding concern. The Committee does not endorse the setting of specific limits on working hours and call schedules and is firmly convinced that such regulation is not consistent with the fundamental principles of surgical education and of surgical care.

Representing the American Board of Surgery, C. James Carrico, MD, reported that the following position related to the resident working environment was approved by the American Board of Surgery at a January 1991 meeting.

> The ABS acknowledges that presently the Resident Working Environment is not optimal in many general surgery residencies. Adverse factors impacting on the working environment include: 1) Undue amount of time spent on tasks that could be better accomplished by other members of the health care team, (e.g. patient transport, laboratory data collection, insurance clearance, and scheduling); 2) Excessive, inappropriate and uncoordinated use of the paging system; 3) Inattention to personal physical needs such as nutrition, adequate sleeping quarters, safety, etc.; 4) Insufficient attention to psychological

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> and emotional stresses such as lack of time for family, indebtedness, recreation and lack of adequate support systems and groups. The residents' problems have been exacerbated by sicker inpatients, a markedly expanded base of knowledge, and multiple sites of care delivery. . .
>
> The ABS strongly believes that limitation of working hours fails to address the overall issue of the residents working environment. Therefore, limitation of working hours alone is insufficient to correct the situation. In addition, such rigid guidelines may adversely affect the quality of patient care and resident education. The ABS endorses the RRC Policy Statement on Working Environment of January 8, 1991. . .
>
> Furthermore, the ABS would recommend the following: 1) The RRC for Surgery should make the status for the residents working environment a high priority in the evaluation of individual programs for accreditation; 2) An in-depth study of the surgical residents environment should be undertaken; 3) In addition to the institutional Graduate Medical Education Committee, there should be constituted an extra departmental, institutional appeal mechanism which may be utilized by residents for the resolution of conflicts; 4) A joint committee of the ABS, RRC for Surgery and American Hospital Association should be formed to develop ways to improve the working environment (e.g. patient care coordinators, debt assistance and support groups for residents and spouses); 5) Education of the public regarding all elements that contribute to high quality of patient care.

Continuing his report from the American Board of Surgery, Dr Carrico indicated that the Board had introduced changes in educational requirements for general surgery at its June 1990 meeting. These changes were prompted by concern regarding fragmentation, fellowship exodus, definition of general surgery, time constraints, funding of education, and issues relating to credentialing. Essentials of the 5-year "flexible" program adopted by the American Board of Surgery follow:

I. Satisfactory completion of a general surgery residency accredited by the Accreditation Council for Graduate Medical Education (ACGME) of not less than 5 years with progressively increasing levels of responsibility.
II. Must have, in a program accredited for a minimum of 5 years, at least 4 years of clinical surgical experience with progressively increasing levels of responsibility. There must be no less than 36 months devoted to the primary components of Surgery (General Surgery) as previously defined. The entire Chief Resident experience must be devoted to the primary components of the specialty of Surgery. No more than 4 months of the Chief Residency may be devoted to any one of the primary components of Surgery.
III. Must have 12 months in the capacity of Chief Resident in General Surgery. The Board considers the terms Chief Resident and Senior Resident to be synonymous and to mean the 12 months in the program in which the resident assumes the ultimate clinical responsibilities for patient care under the supervision of the teaching staff. The majority of the 12 months of Chief Residency must be served in the final year. However, to take advantage of a unique training opportunity in a program during a resident's final year, a portion of the Chief Residency may be served in the next to last year, provided it is no earlier than the fourth clinical year.
IV. Equivalency in the experience of Chief Residents shall be interpreted as equivalency in the responsibility and depth of experience, but not necessarily as equivalency of exposure to the various primary components of general surgery.
V. A training program may be structured to provide in-depth training in either a primary or secondary component of general surgery, provided that all other requirements for surgical training are met, and provided that the residency includes a full 12-month experience with Chief Resident responsibility.
VI. Twelve months of the minimal 5 years may be allocated to nonclinical activities such as laboratory research or basic sciences or the clinical activities in a specialized area of surgical care.

The formal program of the TSDA related to "Criteria for Credit or When does the Resident Really do the Case?" The program was moderated by Fred A. Crawford, MD, and Mark B. Orringer, MD. Participants included John L. Ochsner, MD, representing the Thoracic Surgery RRC and Paul Friedmann, MD, representing the General Surgery RRC; Fred A. Crawford, MD, R. Morton Bolman III, MD, Mark B. Orringer, MD, and Joseph I. Miller, Jr, MD, describing resident involvement in perioperative clinics; and Andrew Gettinger, MD, of the Dartmouth-Hitchcock Medical Center discussing the resident's role in the surgical intensive care unit. In concluding the program, Dr Gay reported on the current TSDA resident match. Enrolled programs total 65 (70% of training programs) and enrolled applicants number 185. The TSDA resident match date is March 15, 1991, for 1993 positions.

The offices of President-Elect, Secretary-Treasurer, and Counselor for the TSDA will be determined at the May 6, 1991, meeting in conjunction with the American Association for Thoracic Surgery in Washington, DC. The nominating committee is chaired by Hendrick B. Barner, MD, with members Hermes C. Grillo, MD, and Benson R. Wilcox, MD.

Gordon F. Murray, MD
Secretary-Treasurer

CORRESPONDENCE

Use of Right Gastroepiploic Artery as a Coronary Artery Bypass Graft

To the Editor:

Currently there is a surge of interest in use of the right gastroepiploic artery as a conduit in myocardial revascularization. By this letter I wish to draw attention to the fact that the right gastroepiploic artery was first used as a direct bypass graft to the right coronary artery in January 1974 by Dr W. Sterling Edwards of Albuquerque, NM [1, 2]. In the decade thereafter use of the right gastroepiploic artery as a conduit in myocardial revascularization sank into oblivion, until in June 1984 Dr John Pym and co-workers [3] of Kingston, Ontario, Canada, used it as a coronary bypass graft to the posterior surface of the heart in patients in whom insufficient saphenous vein of adequate quality was available. Not aware of Dr Sterling's and Dr Pym's use of the right gastroepiploic artery, after preliminary studies in dogs and cadavers in the search of alternative arterial conduits in myocardial revascularization, Dr Juan Carlos Parodi and co-workers of Buenos Aires, Argentina, started clinical use of the right gastroepiploic artery as a coronary artery bypass graft in 1986 (personal communication). Although their experience was never published, they reported it on December 10, 1986, in Punta del Este, Uruguay [4]. As a consequence of the widespread use of this technique in the following years [2, 5–10], Parodi received, in 1989, an award of the Sociedad Argentina de Cirugia Toracica y Cardiovascular.

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References

1. Edwards WS, Blakeley WR, Lewis CE. Technique of coronary bypass with autogenous arteries. J Thorac Cardiovasc Surg 1973;65:272–5.
2. Mills NL, Everson CT. Right gastroepiploic artery: a third arterial conduit for coronary artery bypass. Ann Thorac Surg 1989;47:706–11.
3. Pym J, Brown PM, Charrette EJP, Parker JO, West RO. Gastroepiploic–coronary anastomosis. A viable alternative bypass graft. J Thorac Cardiovasc Surg 1987;94:256–9.
4. Parodi JC, Albertal JA, Fernandez Armaburu D, et al. Utilizacion de la arteria gastroepiploica derecha para la revascularizacion coronaria. Estudio anatomo-patologica y primeros casos clinicos. Informe preliminar. II Congreso Nacional de Angiologia at the XVIII Congreso del Capitulo Latinoamericano of the International Society for Cardiovascular Surgery. Punta del Este, Uruguay, 1986.
5. Carter MJ. The use of the right gastro-epiploic artery in coronary artery bypass grafting. Aust NZ J Surg 1987;57:317–21.
6. Suma H, Fukumoto H, Takeuchi A. Coronary artery bypass grafting by utilizing in situ right gastroepiploic artery: basic study and clinical application. Ann Thorac Surg 1987;44:394–7.
7. Attum AA. The use of the gastroepiploic artery for coronary artery bypass grafts: another alternative. Tex Heart Inst J 1987;14:289–92.
8. Suma H, Takeuchi A, Hirota Y. Myocardial revascularization with combined arterial grafts utilizing the internal mammary and the gastroepiploic arteries. Ann Thorac Surg 1989;47:712–5.
9. Verkkala K, Järvinen A, Keto P, Virtanen K, Lehtola A, Pellinen T. Right gastroepiploic artery as a coronary bypass graft. Ann Thorac Surg 1989;47:716–9.
10. Lytle BW, Cosgrove DM, Ratliff NB, Loop FD. Coronary artery bypass grafting with the right gastroepiploic artery. J Thorac Cardiovasc Surg 1989;97:826–31.

Ventricular Perforation With Valvoplasty

To the Editor:

The recent article by Robertson and associates [1] entitled "Fatal left ventricular perforation during mitral balloon valvoplasty" and ensuing correspondence [2] prompts me to report management of a similar case.

On October 11, 1988, a 67-year-old woman underwent mitral balloon valvoplasty for mitral stenosis. After the mitral valve was successfully dilated, the patient suddenly became hypotensive with signs of cardiac tamponade. A pericardial catheter was inserted, and a salutary hemodynamic response resulted from the withdrawal of approximately 400 mL of blood. This response was transient, and was shortly followed by complete hemodynamic collapse which responded minimally to further pericardial aspiration. Accordingly, the patient was intubated and a left anterior thoracotomy was performed in the catheterization suite. This provided excellent exposure of the typical apical left ventricular perforation, which was simply repaired with a single 2-0 silk horizontal mattress suture. The patient, now hemodynamically stable, was then transported to the operating room where the pericardial cavity and thoracotomy wound were irrigated. The perforation site was hemostatic. The thoracotomy incision was then repaired primarily after the insertion of pericardial and left pleural drainage catheters. After an uneventful recovery that included normal neurological function, the patient was discharged from the hospital on the sixth postoperative day.

In the article by Robertson and associates [1], a fatal outcome is attributed to neurological complications related to delay while awaiting an available operating room. In the responding letter [2], a Bard CPS cardiopulmonary bypass system was used to stabilize the patient for transfer to the operating room. The latter patient required mitral valve replacement as well as ventricular perforation repair, and had a successful outcome.

Although I agree that operating room availability is an important issue in this era of interventional cardiology, I believe that the case presented here illustrates the importance of surgical standby in all senses of the word. Emphasis should be placed on the presence of the surgeon, rather than methods or resources, so that *all* options are available for the injured patient. Emergency left anterior thoracotomy is a rapid method to achieve hemodynamic stability in a life-threatening situation and was accomplished in the patient reported here with a minimum of "technology." It provides excellent exposure of the probable site of injury due to balloon mitral valvoplasty, and is unlikely to increase the risk to which the patient has already been exposed. Infectious complications are highly unlikely and could be further minimized by repairing the thoracotomy wound before a standard approach to definitive mitral valve operation is undertaken, if it is required.

Although percutaneous cardiopulmonary bypass was used successfully in a single patient with this complication, it must be considered a complicated and indirect approach to the underlying problem in this clinical setting. Its use may expose the patient to additional hazards, the most important being further delay in definitive therapy. I would recommend that the employment of percutaneous cardiopulmonary bypass be made in consultation

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with a thoracic surgeon, who may be able to provide a more rapid and definitive solution.

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References

1. Robertson JM, de Virgilio C, French W, Ruiz C, Nelson RJ. Fatal left ventricular perforation during mitral balloon valvoplasty. Ann Thorac Surg 1990;49:819–21.
2. Aaron BL, Alyono D. Ventricular perforation with valvoplasty [Letter]. Ann Thorac Surg 1990;50:1022.

Reply

To the Editor:

I am not surprised to find another institution with an injury similar to the one we reported [1]. This second response to our paper underscores the fact that *mitral balloon valvoplasty carries with it a serious risk of ventricular perforation.* Looking at the reports in the medical literature, one would not recognize this complication as a very likely occurrence. However, these three reports plus several others that I have personally become aware of clearly support the fact that this procedure is potentially dangerous and must have surgical backup.

My colleagues and I are in agreement with Dr Smith's emphasis on the "presence of the surgeon" and the availability of all the appropriate tools he or she may require whenever one of these procedures is performed. Presently, many catheterization laboratories use the word "standby" to mean that the surgical team has been *informed* of the procedure and that if a complication should arise their team could be summoned from wherever they might be. I agree that this is inadequate and that when such a potentially dangerous procedure is performed, a more formal surgical arrangement should be made.

In the case report by Drs Aaron and Alyono, the Bard CPS system was useful in the salvage of their patient [2]. We now hear from Dr Smith's group at Duke that a left thoracotomy was the procedure they selected that provided them with very nice salvage of their patient. However, as I previously pointed out, at the Harbor/UCLA Medical Center we did not have the Bard system, and in reference to the left anterior thoracotomy, our catheterization laboratory is in the basement of the hospital with the operative theater two floors above. We had no surgical equipment in the catheterization laboratory and were called to see the patient only after multiple cardiologic procedures were attempted. For us, the simplest thing to do was take the patient directly to the operating room.

All three of these cases point out the importance of having a firm commitment and understanding between the departments of cardiothoracic surgery and cardiology before any major invasive procedure, such as mitral balloon valvoplasty, is attempted. All members of the team (both surgical and medical) and their appropriate equipment should be immediately available at the start of such a procedure. In addition, the procedure should be performed in an area that will allow for the appropriate means of rectifying any complication. In Dr Smith's case, this would be in an area that is well illuminated, with the appropriate surgical equipment and staff so that an anterior thoracotomy could be performed. In addition, if the patient is still awake, one must consider the anesthetic requirements for performing an anterior thoracotomy on a patient who may be fully aware of what is happening. This latter point was not addressed by Dr Smith, but I am sure at the Duke facility appropriate anesthetic considerations were given to the patient.

In summary, I strongly believe and I hope that our three cases point out to the community at large that mitral balloon valvoplasty is not a benign procedure. It is instead a procedure that may be accompanied by potentially lethal complications. Therefore, at institutions where the procedure is practiced there must be in place a plan of action that allows for a true coordinated response between both medical and surgical departments should any complications occur.

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References

1. Robertson JM, de Virgilio C, French W, Ruiz C, Nelson RJ. Fatal left ventricular perforation during mitral balloon valvoplasty. Ann Thorac Surg 1990;49:819–21.
2. Aaron BL, Alyono D. Ventricular perforation with valvoplasty [Letter]. Ann Thorac Surg 1990;50:1022.

Calcium in Neonatal Cardioplegia

To the Editor:

The study by Zweng and co-workers [1] examining the optimal calcium concentration in cardioplegic solutions for neonatal hearts addresses the serious clinical question of the appropriate dosage of this important cation. However, their study method using normothermic ischemia to develop this dose-response curve raises strong questions as to its relevance, because hypothermic ischemia is almost universally applied in clinical practice.

Yamamoto and associates [2] performed the first calcium dose-response studies on mature hearts at St. Thomas' Hospital in 1984, finding the concentration 1.2 mmol/L optimal for normothermic ischemia. Because hypothermia such as that used clinically is known to induce membrane lipid phase transitions, as well as to influence the activity of membrane-bound processes such as enzymes and receptors, it was believed important to reevaluate the calcium dose-response characteristics in cardioplegic solution using lengthy hypothermic ischemia. In our laboratory, using the same isolated working rat heart model as Yamamoto and associates, we found the sharp calcium dose-response curve was shifted downward when studied with 5 hours of hypothermic (20°C) ischemia. Under these conditions, the optimal calcium concentration in St. Thomas' Hospital cardioplegic solution was considerably lower at 0.6 mmol/L [3, 4]. Later similar studies by the St. Thomas' Hospital group [5], also using hypothermic ischemia, confirmed our optimal calcium dose and support our contention that cold significantly changes results. Consequently we must question the clinical usefulness of normothermic ischemia studies with cardioplegic solutions.

Furthermore, because cardioplegic studies in mature animals may not necessarily reflect results that are found in the immature heart, calcium dose-response curves require redefinition in the neonatal animal. The recent study of Zweng and co-workers [1] in neonatal rabbit hearts unfortunately was performed using normothermic ischemia. Baker and co-workers [6] found in neonatal rabbit hearts exposed to 6 hours of hypothermic (14°C) ischemia that the calcium dose-response curve also was shifted downward with cold such that 0.3 mmol/L was the optimal calcium concentration in St. Thomas' Hospital cardioplegic solution. The results of Baker and co-workers [6] in the neonatal heart are remarkably similar to those found in our laboratory in mature hearts.

Although I commend Zweng and associates for their elegant study, their choice of normothermic ischemia for testing experimental groups substantially diminishes the clinical relevance of their results. Indeed, the changes in dose-response characteristics experimentally shown to occur with hypothermia seriously question the validity of performing similar studies at 37°C on any cardioplegic component.

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References

1. Zweng TN, Iannettoni MD, Bove EL, et al. The concentration of calcium in neonatal cardioplegia. Ann Thorac Surg 1990;50: 262–7.
2. Yamamoto F, Braimbridge MV, Hearse DJ. Calcium and cardioplegia. The optimal calcium content for the St. Thomas' Hospital cardioplegic solution. J Thorac Cardiovasc Surg 1984; 87:908–12.
3. Robinson LA, Harwood DL. Lower calcium improves protection with St. Thomas' Hospital cardioplegic solution during hypothermic ischemia [Abstract]. J Mol Cell Cardiol 1988; 20(Suppl 5):S–46.
4. Robinson LA, Harwood DL. Lowering the calcium concentration in St. Thomas' Hospital cardioplegic solution improves protection during hypothermic ischemia. J Thorac Cardiovasc Surg 1991;101:314–25.
5. Takahashi A, Chambers DL, Braimbridge MV, Hearse DJ. Long-term hypothermic preservation of the heart: the optimal concentration of calcium in the St. Thomas' Hospital cardioplegic solution [Abstract]. J Mol Cell Cardiol 1989;21(Suppl 2):S–121.
6. Baker JE, Baker EJ, Olinger GW. Protection of the ischemic immature myocardium: the optimal calcium content of the St. Thomas' II cardioplegic solution [Abstract]. J Mol Cell Cardiol 1990;22(Suppl 5):S–20.

Reply

To the Editor:

In a recent study from our laboratory, normothermic ischemic conditions were used to evaluate the optimal calcium concentrations in St. Thomas' cardioplegia for the neonatal rabbit heart [1]. Our experimental protocol has been questioned by Dr Robinson because normothermic ischemia is rarely used in the operating room. Hence, in Dr Robinson's view, the results that we reported have limited clinical relevance. We readily acknowledge now, as we did in our report, that there are differences between normothermia and hypothermia. The objective of our study, however, was not to simulate operating room conditions. Rather, it was to address another in a series of specific and fundamental issues in a well-defined experimental model that has been used in many previous investigations. It is well established that there are important basic differences in structure, function, and metabolism of immature and mature hearts and that useful information may be obtained from studies examining the effect of various cardioplegic compositions at any temperature. Furthermore, there is ample precedent in the literature (including this journal) for normothermic ischemic studies in the immature heart. Although the main reason for using normothermia is practical (ie, it reduces the experimental time to a manageable length), recent interest in warm induction cardioplegia suggests that normothermia may indeed have an important role in neonatal protective strategies [2]. Consequently, the effects of various calcium concentrations at 37°C may well be clinically relevant.

Given that Dr Robinson's results, reported recently [3], are at variance with our own, it is not surprising that his evaluation of our paper was largely critical. Disagreement is a useful part of the scientific process, but we think that his criticism of the use of normothermic ischemia is unwarranted. We look forward to hearing more about the optimal calcium concentration in cardioplegia from Dr Robinson and other investigators in settings that are clinically useful or mechanistically oriented.

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References

1. Zweng TN, Ianettoni MD, Bove EL, et al. The concentration of calcium in neonatal cardioplegia. Ann Thorac Surg 1990;50: 262–7.
2. Williams WG, Rebeyka IM, Tibshirani RJ, et al. Warm induction blood cardioplegia in the infant: a technique to avoid rapid cooling myocardial contracture. J Thorac Cardiovasc Surg 1990;100:896–901.
3. Robinson LA, Harwood DL. Lowering the calcium concentration in St. Thomas' Hospital cardioplegic solution improves protection during hypothermic ischemia. J Thorac Cardiovasc Surg 1991;101:314–25.

Acute Vascular Trauma

To the Editor:

I am indebted to Drs McLean and McManus [1] and Dr Pate [2] for bringing to our attention a subject seldom discussed and infrequently seen in civilian practice: injuries to major arteries from the aorta to the neck and upper extremities. I concur with their diagnostic and therapeutic recommendations, emphasizing that such an approach is valid for both penetrating and blunt injuries to these vessels.

A recent case of chest trauma serves to highlight three personal observations: first, one must always remember that blunt chest trauma can produce bilateral injury to vessels originating in the aorta; second, angiography by itself may not be sufficient to fully demonstrate the extent of these injuries; and third, the application of photographic subtraction techniques to angiographic film can be an invaluable aid in the interpretation of findings before the contemplated surgical repair.

A 23-year-old male driver of a pick-up truck was involved in a high-speed, head-on collision with another vehicle. Prompt resuscitative measures restored his hemodynamic status. Multiple bruises, a pulseless right arm, and a fractured right patella were noticed in an otherwise alert individual. Chest roentgenogram showed multiple fractured ribs, a fractured sternum, bilateral pneumothoraces, and widening of the upper right mediastinum. An arch angiogram (Fig 1) established the integrity of the thoracic aorta and showed complete transection of the right subclavian artery with reconstruction of the distal brachial artery through collaterals. The left subclavian artery was interpreted as being tortuous in its midportion with an otherwise intact distal vessel. The same night, the injury was approached through a median sternotomy incision with a right supraclavicular extension, and the totally transected right subclavian artery was repaired with a reversed segment of saphenous vein with restoration of peripheral pulses.

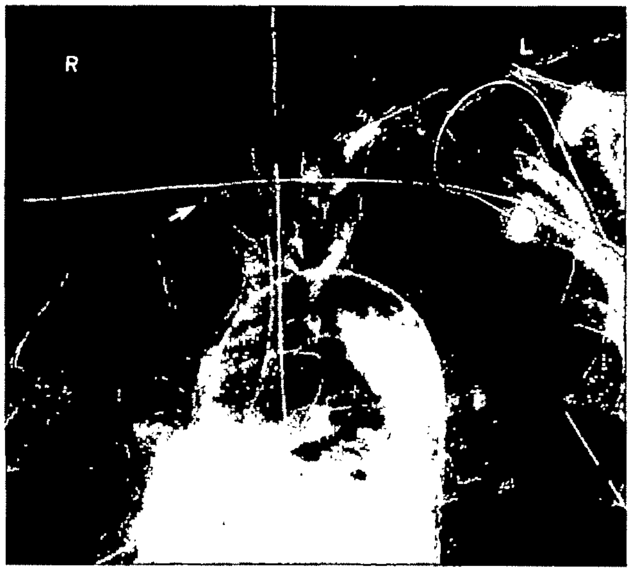

Fig 1. Aortogram showing transection of right subclavian artery at its origin from the innominate artery (arrow) *and poor definition of the left subclavian artery at its midportion.*

Further review of the angiograms with the photographic subtraction technique [3] clearly demonstrated an acute false aneurysm of the left subclavian artery not readily identifiable on the original angiogram (Fig 2). The patient was reoperated on through the same median sternotomy with additional left supraclavicular and second left intercostal space incisions. Proximal and distal ligation of the false aneurysm was carried out with the interposition of a saphenous vein graft to restore distal pulses. The postoperative course was uneventful and the patient is well 6 months after the accident.

Although blunt traumatic injuries to the subclavian artery are rare, the even more unusual possibility of the lesion being bilateral must be kept in mind as the present case illustrates. At the moment, there appears to be general agreement on an adherence to the principles of diagnosis and management of these cases [4, 5]. A simple and readily available technical manipulation of the sometimes unclear angiograms by photographic subtraction may contribute in many cases to make diagnostically important information easier to see. In the case reported here, it prevented a concomitant injury of the left subclavian artery from remaining undiagnosed and untreated.

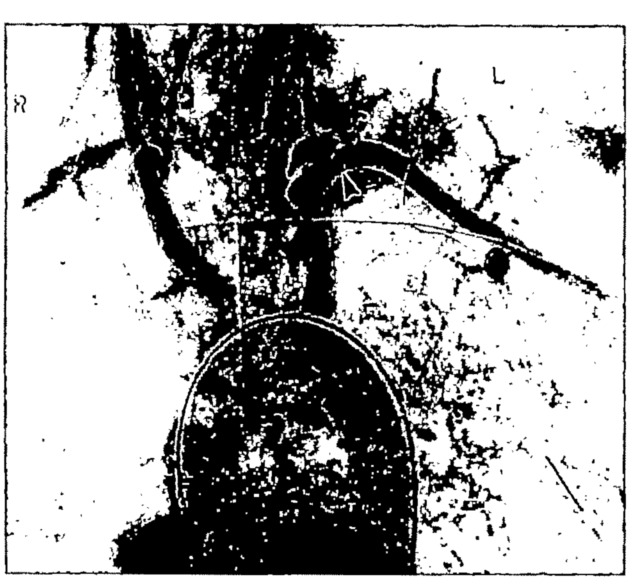

Fig 2. Subtraction print of x-ray film in Figure 1: an associated false aneurysm of the left subclavian artery is now clearly visible (arrow).

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References

1. McLean TR, McManus RP. Penetrating trauma involving the innominate artery. Ann Thorac Surg 1991;51:113–5.
2. Pate JW. Invited commentary on [1]. Ann Thorac Surg 1991; 51:113–5.
3. Christensen EE. The subtraction technique. In: Christensen EE. Introduction to the physics of diagnostic radiology. 3rd ed. Philadelphia: Lea & Febiger, 1984:290–4.
4. Mattox KL. Symposium—new approach in vascular trauma. J Vasc Surg 1988;7:725–39.
5. Spence RK, Alexander JB, Camishion RC. Blunt rupture of thoracic great vessels. Trauma Q 1990;6:27–41.

Management of Endobronchial Hemorrhage

To the Editor:

We read with interest a recent article and invited commentary by Purut and associates and Tyers, respectively [1], regarding the intraoperative management of Swan-Ganz catheter–induced pulmonary artery perforation and endobronchial hemorrhage. As pointed out by these authors, the protection of contralateral and uninvolved lung from asphyxia is of paramount importance; this could be achieved either by placement of an endobronchial blocker or by double-lumen endotracheal intubation as reported previously by us in this journal [2]. Obviously, control of pulmonary hemorrhage using pulmonary artery venting to allow selective placement of an endobronchial blocker under the guidance of flexible bronchoscopy presents a unique situation for the ingenious intraoperative intervention described by Purut and associates.

However, a few comments concerning the natural history as well as ultimate management of the complications of Swan-Ganz catheter–induced pulmonary artery perforation appear not adequately addressed by these authors and are worthy of reiteration here.

As previously stated [2], nonsurgical management of pulmonary artery perforation could often be successful, because of the involvement of a low-pressure vascular system. Once the airway is protected, modification of risk factors such as lowering of pulmonary artery hypertension, reversal of anticoagulation, and sedation would frequently lead to spontaneous cessation of bleeding and early extubation. However, rebleeding and the development of false aneurysm are the major drawbacks of nonresectional management. The precise incidences are unknown because of the scarcity of long-term survivors. Of those that were reported, the occurrence appeared to be substantially high and often with fatal outcome. As a result, we advocate that those who survive initial nonresectional management of pulmonary artery hemorrhage should have a pulmonary arteriogram to evaluate for residual defect or false aneurysm. It would be advisable to perform transcatheter embolization to occlude such defects if demonstrable. Transcatheter embolization technique [3] has been found to be quite effective with low risk.

The patient reported by us, in whom a false pulmonary artery aneurysm developed after successful nonresectional management of a Swan-Ganz catheter–induced pulmonary hemorrhage, subsequently underwent transcatheter embolization. The patient is still alive and well 2 years after the incident without any signs of residual false aneurysm.

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References

1. Purut CM, Scott SM, Parharu JV, Smith PK. Intraoperative management of severe endobronchial hemorrhage. Ann Thorac Surg 1991;51:304–7.
2. Feng WC, Singh AK, Drew T, Donat T. Swan-Ganz catheter-induced massive hemoptysis and pulmonary artery false aneurysm. Ann Thorac Surg 1990;50:644–6.
3. Davis SD, Neithamer CD, Schreiber TS, Sos TA. False pulmonary artery aneurysm induced by Swan-Ganz catheter: diagnosis and embolotherapy. Radiology 1987;164:741–2.

Repair of Catheter-Induced Perforation of the Pulmonary Artery

To the Editor:

Pulmonary artery rupture is a life-threatening complication of Swan-Ganz catheters employed during cardiac operations. In the recent report of Purut and associates [1], and the invited commentary of Tyers [2], the management of this condition was extensively discussed. One additional option in management, direct arterial repair, warrants consideration. Our experience with 1 case is reported.

A 60-year-old woman with a history of a large anterior myocardial infarction and chronic obstructive lung disease was seen to have unstable angina and severe congestive heart failure. Cardiac catheterization demonstrated a cardiac index of 1.9 $L \cdot min^{-1} \cdot m^{-2}$, left ventricular ejection fraction of 0.05, left ventricular end-diastolic pressure of 25 mm Hg, and a large left ventricular aneurysm. The patient underwent left ventricular aneurysmectomy and aortocoronary grafting to the first obtuse marginal artery with placement of a 7-mm Swan-Ganz catheter before induction of anesthesia. During weaning from bypass, blood was noted in the endotracheal tube. After resumption of cardiopulmonary bypass the right pleural cavity was opened and approximately 2 L of intrapleural blood was found. Dissection in the major fissure revealed a 1.5-cm tear in the pulmonary artery. Repair with a continuous 4-0 polypropylene suture was performed. Pulmonary resection was not required. An intraaortic balloon pump was inserted to facilitate weaning from bypass. The postoperative course was complicated by prolonged respiratory insufficiency. The patient was discharged home on the 29th postoperative day.

Because the precise site of arterial perforation is not visible in most cases of catheter-induced pulmonary artery rupture [3], management usually involves either pulmonary resection or a variety of conservative measures [4]. Successful control of hemorrhage with preservation of pulmonary function makes arterial repair an attractive option in select patients.

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References

1. Purut CM, Scott SM, Parham JV, Smith PK. Intraoperative management of severe endobronchial hemorrhage. Ann Thorac Surg 1991;51:304–7.
2. Tyers GFO. Invited commentary on [1]. Ann Thorac Surg 1991;51:304–7.
3. Connors JP, Sandza JG, Shaw RC, Wolff GA, Lombardo JA. Lobar pulmonary hemorrhage. An unusual complication of Swan-Ganz catheterization. Arch Surg 1980;115:883–5.
4. Fleisher AG, Tyers GFO, Manning GT, Nelems B. Management of massive hemoptysis secondary to catheter-induced perforation of the pulmonary artery during cardiopulmonary bypass. Chest 1989;95:1340–1.

Mitral Prosthetic Replacement in Small Left Atria

To the Editor:

We were surprised to read an article in the November 1990 issue of *The Annals* entitled "Mitral Prosthetic Replacement in Small Left Atria" [1]. A similar technique was described 9 years ago in an article that also appeared in *The Annals* [2].

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References

1. Campanella C, Cameron E, Feilberg VL. Mitral prosthetic replacement in small left atria. Ann Thorac Surg 1990;50:836–7.
2. Brawley RK. Improved exposure of the mitral valve in patients with a small left atrium. Ann Thorac Surg 1980;29:179–81.

Reply

To the Editor:

The surprise of Dr Balasundaram and Dr Duran is understood. We are bound to admit the inadequacy of our search of the literature because, unaware of Dr R. K. Brawley's communication of 10 years previously [1], we described what we believed to be a new modification of the Dubost approach for prosthetic replacement of the difficult mitral valve.

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1. Brawley RK. Improved exposure of the mitral valve in patients with a small left atrium. Ann Thorac Surg 1980;29:179–81.

Nonsurgical Treatment of Carcinoid Heart Disease

To the Editor:

I read with interest the case report by Fetherston and Davis [1] on the surgical treatment of carcinoid heart disease. There is now an alternative nonsurgical form of treatment of carcinoid heart disease, namely, percutaneous balloon dilation of stenosed pulmonic and tricuspid valves.

Although balloon valvuloplasty will not take care of the tricuspid regurgitant lesion in carcinoid heart disease, relief of pulmonic stenosis by percutaneous balloon dilation will ameliorate the degree of tricuspid regurgitation. Admittedly the major functional defect in carcinoid heart disease is tricuspid regurgitation; tricuspid stenosis may also occur [2]. Percutaneous balloon dilation of the tricuspid valve has been shown to be safe and effective for tricuspid stenosis caused by carcinoid [3].

Concurrent percutaneous balloon valvuloplasty for combined pulmonic and tricuspid stenoses not only is feasible [4], but spares the patient with a malignant disease from a major open heart operation.

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References

1. Fetherston GJ, Davis BB. Surgical management of carcinoid heart disease. Ann Thorac Surg 1991;51:493–4.
2. Hurst J. The heart. 7th ed. New York: McGraw Hill, 1990:856.
3. Mullins PA, Hall JA, Shapiro LM. Balloon dilatation of tricuspid stenosis caused by carcinoid heart disease. Br Heart J 1990;63:249–50.
4. Chen CR, Lo ZX, Huang ZD, Cheng TO. Concurrent percutaneous balloon valvuloplasty for combined tricuspid and pulmonic stenoses. Cathet Cardiovasc Diagn 1988;15:55–60.

Circulatory Support 1991

The Second International Conference on Circulatory Support Devices for Severe Cardiac Failure

San Francisco Marriott Hotel, San Francisco, California
November 15–17, 1991 (weekend meeting)

Circulatory Support 1991 will be a comprehensive multidisciplinary meeting focusing on the clinical applications of the entire spectrum of circulatory support devices. Surgeons, cardiologists, anesthesiologists, intensivists, perfusionists, engineers, and operating room and intensive care nurses are encouraged to attend as individuals or as a team.

The meeting is sponsored by The Society of Thoracic Surgeons under the direction of its Ad Hoc Committee on Circulatory Support and Thoracic Transplantation.

Registration fees for this meeting are: Physician, $250.00; Perfusionist/Engineer, $175.00; Nurse, $125.00.

For this weekend meeting, the Saturday morning segment entitled "Problem Cases" will include panel and audience discussions of four major subject areas: patient selection; anticoagulation management, bleeding, and thromboembolic risk; infections—prophylaxes and treatment; and management of secondary organ dysfunction. An outstanding international panel has been chosen to represent a broad spectrum of opinions for each subject.

Late Saturday morning and early afternoon, video sessions on the working details and proposed indications for support devices that are currently in use or development will be presented. A report of the current circulatory support device registry will be given. Breakout sessions of smaller groups will follow and focus on how to use external nonpulsatile circulatory support, external pulsatile circulatory support, and internal pulsatile circulatory support.

The Sunday sessions from 7:45 AM to 1:00 PM will be devoted to state-of-the-art presentations covering: emergency resuscitation techniques, heparinless bypass, the Hemopump experience, postoperative use of the Biopump, the VAD experience in Japan, optimizing hemodynamics and assessing myocardial recovery, right heart management during LVAD support, circulatory support in children, bridge to transplantation with the Thoratec VAD and with the Symbion TAH, chronic support with the TCI left ventricular assist system, the Novacor left ventricular assist system, and the Penn State TAH.

Poster presentations concerning a wide variety of subjects related to circulatory support as well as commercial exhibits demonstrating currently available devices will be available during breaks. Full CME credit will be provided for attendees.

The deadline for submission of poster abstracts is August 1, 1991. For further information and guidelines on poster abstract submission and other available meeting information, contact: The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; telephone: (312) 644-6610.

PROGRAM

Saturday, November 16

8:00–8:15	**Welcome and Opening Remarks** D. Glenn Pennington, St. Louis, MO
	Problem Case-Oriented Panels
8:15–8:55	**Panel I: Patient Selection** *Moderator*: D. Glenn Pennington, St. Louis, MO *Panelists*: David J. Farrar, San Francisco, CA; Daniel Loisance, Paris, France; Walter E. Pae, Jr, Hershey, PA; and Robert W. Emery, Minneapolis, MN
8:55–9:15	**Registry Report** Walter E. Pae, Jr, Hershey, PA
9:15–10:05	**Video Session I** *Discussion Leader*: W. Gerald Rainer, Denver, CO
10:05–10:50	**Break to Visit Posters/Exhibits**
10:50–11:40	**Video Session II** *Discussion Leader*: Wilbert J. Keon, Ottawa, Canada
11:40–12:30	**Video Session III** *Discussion Leader*: Ernst Wolner, Vienna, Austria

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12:30–1:30 **Lunch**

1:40–2:40 **"How To" Panel Session I**

1. Nonpulsatile Circulatory Support
   Moderator: George J. Magovern, Pittsburgh, PA

   Panelists: Richard K. Wampler, Rancho Cordova, CA; Leonard A. R. Golding, Cleveland, OH; and Lyle D. Joyce, Minneapolis, MN
2. External Pulsatile Circulatory Support
   Moderator: J. Donald Hill, San Francisco, CA

   Panelists: Yukiyasu Sezai, Tokyo, Japan; Roland Hetzer, Berlin, Germany; and Robert A. Guyton, Atlanta, GA
3. Internal Pulsatile Circulatory Support
   Moderator: Peer M. Portner, Oakland, CA

   Panelists: William A. Baumgartner, Baltimore, MD; Christian Cabrol, Paris, France; and O. Howard Frazier, Houston, TX

1:40–2:40 **Cardiac Nursing Session**
Nursing Care of the Patient on Mechanical Circulatory Support
Moderator: Julie Shinn, Stanford, CA

1. Transfer of VAD Patients to Non-Critical Care Areas
   Nancy Abou-Awdi, Houston, TX
2. Nutritional Support and Activity Guidelines
   Jill Ley, San Francisco, CA
3. Infection Control Measures
   Jane Reedy, St. Louis, MO
4. Psychosocial Aspects of Care
   Don Rountree, Louisville, KY

2:45–3:45 **"How To" Panel Session II**

1. Nonpulsatile Circulatory Support
   Moderator: George Paul Noon, Houston, TX

   Panelists: Jack J. Curtis, Columbia, MO; Charles Henry Moore III, San Antonio, TX; and Michael S. Sweeney, Houston, TX
2. External Pulsatile Circulatory Support
   Moderator: Charles-Julien Hahn, Arzier, Switzerland

   Panelists: William L. Holman, Birmingham, AL; Jack G. Copeland III, Tuscon, AZ; and Gerard Champsaur, Lyon, France
3. Internal Pulsatile Circulatory Support
   Moderator: Philip E. Oyer, Stanford, CA

   Panelists: Robert L. Kormos, Pittsburgh, PA; Terence Lewis, London, England; and Roque P. Pifarre, Chicago, IL

3:45–4:30 **Break**
Visit Posters and Exhibits

4:40–5:10 **Panel II: Anticoagulation**
Moderator: Jack G. Copeland III, Tucson, AZ

Panelists: O. Howard Frazier, Houston, TX; Lawrence R. McBride, St. Louis, MO; Marko Turina, Zurich, Switzerland; and Christian Cabrol, Paris, France

5:10–5:50 **Panel III: Infections—Prophylaxis and Treatment**
Moderator: J. Donald Hill, San Francisco, CA

Panelists: Bartley P. Griffith, Pittsburgh, PA; Charles-Julien Hahn, Arzier, Switzerland; and Paul Didisheim, Bethesda, MD

5:50–6:30 **Panel IV: Management of Secondary Organ Dysfunction**
Moderator: William S. Pierce, Hershey, PA

Panelists: John M. Armitage, Pittsburgh, PA; James J. Hershon, San Francisco, CA; Walter P. Dembitsky, San Diego, CA; and George Paul Noon, Houston, TX

Sunday, November 17

6:40–7:40 **Special Breakfast Panel V: Long-Term Biventricular**
Moderator: Charles-Julien Hahn, Arzier, Switzerland

Panelists: William S. Pierce, Hershey, PA; Donald B. Olson, Salt Lake City, UT; Kenneth Butler, Rancho Cordova, CA; and Robert T. V. Kung, Danvers, MA

7:45–9:20 **State of the Art I**
Moderator: Frank C. Spencer, New York, NY

1. Emergency Resuscitation With ECMO
   Walter P. Dembitsky, San Diego, CA
2. Circulatory Support With Heparinless CPB
   Per Olsson, Stockholm, Sweden
3. Hemopump Clinical Results and Applications
   Richard K. Wampler, Rancho Cordova, CA
4. Biopump in Postoperative Circulatory Support
   George J. Magovern, Pittsburgh, PA
5. VAD Experience (Postcardiotomy and AMI) in Japan
   Hisateru Takano, Osaka, Japan

9:20–10:05 **Break**

10:05–11:40 **State of the Art II**
Moderator: Michael E. DeBakey, Houston, TX

6. Optimizing Hemodynamics and Assessing Myocardial Recovery
   George Paul Noon, Houston, TX
7. Circulatory Support With Acute Myocardial Infarction Shock
   Ernst Wolner, Vienna, Austria
8. Status of Circulatory Support in Children
   D. Glenn Pennington, St. Louis, MO
9. World Experience With Skeletal Muscle Cardiac Assist
   James A. Magovern, Pittsburgh, PA
10. New Approaches to Cardiomyoplasty
    Adib D. Jatene, Sao Paulo, Brazil

12:00–1:35 **State of the Art III**
Moderator: Norman E. Shumway, Stanford, CA

11. Right Heart Management During LVAD
    Bartley P. Griffith, Pittsburgh, PA
12. Bridge to Transplant With the Thoratec VAD
    J. Donald Hill, San Francisco, CA
13. Bridge to Transplant With the Symbion J7 TAH
    Christian Cabrol, Paris, France
14. Chronic Support With the TCI LVAS
    O. Howard Frazier, Houston, TX
15. Chronic Support With the Novacor LVAS
    Peer M. Portner, Oakland, CA

2:00 **Close of Main Session**

2:30–4:00 **Regulatory Issues Session**
How Much Do We Need to Know Before Approving a Ventricular Assist Device?
Moderator: J. Donald Hill, San Francisco

Panelists: Betty Lemperle, FDA Reviewer; Mark Levinson, FDA Advisory Committee Member; Victor Poirier, Industry Perspective (Thermo Cardiosystems, Inc); and D. Glenn Pennington, Clinical Perspective

4:00–5:00 **Question and Answer Session**

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KEY TO ABBREVIATIONS USED FOR ARTICLE CLASSIFICATION

* = Original Article
AN = Announcement
CL = Classics in Thoracic Surgery
CR = Case Report
CP = Correspondence
CT = Collective Review
CV = Current Review
DI = Discussion
ED = Editorial
HW = How to Do It
IC = Invited Commentary
KR = Key References
PA = Presidential Address
RE = Report
RV = Review of Recent Books

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Cowgill LD. The Fontan procedure: a historical review. 1991;51:1026–30,CL
Cox JL. *see* Ferguson & Cox. 1991;51:723–32*
Craig B. *see* McCrory, Craig, & others. 1991;51:821–2,CR
Cremonesi A. *see* Noera, Sanguinetti, & others. 1991;51:320–2,CR
Crittenden MD, Roberts CS, Rosa L, Vatsia SK, Katz D, Clark RE, Swain JA. Brain protection during circulatory arrest. 1991;51:942–7*
Cronin J. *see* Lahey, Meyer, & others. 1991;51:299–301,CR
Crooke GA. *see* Grossi, Colvin, & others. 1991;51:484–7,CR
Crupi G. *see* Merlo, De Tommasi, & others. 1991;51:227–31*
Curtis JJ. *see* Landreneau, Hazelrigg, & others. 1991;51:973–8*
Curtis JJ. *see* Landreneau, Hinson, & others. 1991;51:473–5,CR
Curtis JJ. *see* Landreneau, Marshall, & others. 1991;51:128–30,CR
Cusimano RJ. *see* Salerno, Christakis, & others. 1991;51:1023–5,HW

Czer LSC. *see* Blanche, Segalowitz, & others. 1991;51:670–2,CR
Czorniak M. *see* Lahey, Meyer, & others. 1991;51:299–301,CR

Dadourian BJ, Perloff JK, Drinkwater DC, Child JS, Mulder DG. Double outlet left ventricle—long survival after surgical correction. 1991;51:159–60,CP
Daggett WM. *see* Steinberg, Doherty, & others. 1991;51:620–9*
D'Agostino RS. *see* Ponn, Blancaflor, & others. 1991;51:605–9*
Daily PO, Dembitsky WP, Daily RP. Dissectors for pulmonary thromboendarterectomy. 1991;51:842–3,HW
Daily PO, Kinney TB. Optimizing myocardial hypothermia: II. Cooling jacket modifications and clinical results. 1991;51:284–9*
Daily PO. *see* Kinney, Daily, & others. 1991;51:278–83*
Daily RP. *see* Daily, Dembitsky, & others. 1991;51:842–3,HW
Daly BDT, Faling LJ, Diehl JT, Bankoff MS, Gale ME. Computed tomography–guided minithoracotomy for the resection of small peripheral pulmonary nodules. 1991;51:465–9*
Daly RC, Trastek VF, Pairolero PC, Murtaugh PA, Huang M-S, Allen MS, Colby TV. Bronchoalveolar carcinoma factors affecting survival. 1991;51:368–77*
Damle A. *see* Browdie, Bernstein, & others. 1991;51:290–2*
Daniëls O. *see* van Son, Daniëls, & others. 1991;51:344,CP
Dapper F. *see* Boldt, Zickmann, & others. 1991;51:610–5*
Dapper F. *see* Boldt, Zickmann, & others. 1991;51:747–53*
Datz FL. *see* Morton, Karwande, & others. 1991;51:759–63*
Davies SW, Bailey J, Wedzicha JA, Rudd RM. Complement activation and lung permeability during cardiopulmonary bypass. 1991;51:695–6,CP
Davis BB. *see* Fetherston & Davis. 1991;51:493–4,CR
Davis RK. *see* Morton, Karwande, & others. 1991;51:759–63*
de Leval MR. *see* Snir, de Leval, & others. 1991;51:979–82*
De Tommasi SM. *see* Merlo, De Tommasi, & others. 1991;51:227–31*
DeBakey ME. *see* Kotliar, Smart, & others. 1991;51 987–91*
Deeb GM. *see* Bolling, Putnam, & others. 1991;51:52–5*
DelRossi AJ. *see* Cilley, Cernaianu, & others. 1991;51:504–5,HW
Dembitsky WP. *see* Daily, Dembitsky, & others. 1991;51:842–3,HW
Denenberg AG. *see* Steinberg, Doherty, & others. 1991;51:620–9*
Denning L. *see* Novick, Reid, & others. 1991;51:853–9,CV
Depan HJ. *see* Guth, Gouge, & others. 1991;51:837–9,CR
DeShong JL. *see* Graeber, Collins, & others. 1991;51:901–5*
Deslauriers J. *see* Awad, Deslauriers, & others. 1991;51:534–40*
Detterbeck FC. *see* Lambert, Egan, & others. 1991;51:924–30*
Deveze JL. *see* Bex, Grande, & others. 1991;51:694–5,CP
Di Eusanio G. Mazzola A, Gregorini R, Esposito G, Di Nardo W, Di Manici G, Villani C. Left ventricular aneurysm secondary to Behçet's disease. 1991;51:131–2,CR
Di Manici G. *see* Di Eusanio, Mazzola, & others. 1991;51:131–2,CR
Di Nardo W. *see* Di Eusanio, Mazzola, & others. 1991;51:131–2,CR
Diehl JT. *see* Breckwoldt, Genco, & others. 1991;51:959–63*
Diehl JT. *see* Daly, Faling, & others. 1991;51:465–9*
Diehl JT. *see* Sindhi, Belisle, & others. 1991;51:676–7,HW
DiSesa VJ. Art and science in the management of endocarditis. 1991;51:6–7,ED
DiSesa VJ. *see* Peigh, DiSesa, & others. 1991;51:102–4*
Doherty NE. *see* Steinberg, Doherty, & others. 1991;51:620–9*
Donlon JB. *see* Yadava, Hodge, & others. 1991;51:189–93*
Donnelly RJ. Esophagogastrectomy via left thoracotomy. Reply. 1991;51:163,CP
D'Orazio SA. *see* Naunheim, Kesler, & others. 1991;51:547–51*
Doty DB. Supravalvar aortic stenosis. 1991;51:886–7,ED
Douville EC, Sade RM, Fyfe DA. Hemi-Fontan operation in surgery for single ventricle: a preliminary report. 1991;51:893–900*
Doyle EF. *see* Grossi, Colvin, & others. 1991;51:484–7,CR
Drinkwater DC. *see* Dadourian, Perloff, & others. 1991;51:159–60,CP
Duke DJ. *see* Chopra, Duke, & others. 1991;51:840–1,CR
Duncan NF. *see* Robertson, Penkoske, & others. 1991;51:73–5*
Dunn JM. Jatene's arterial repair for transposition of the great vessels. 1991;51:511–4,CL
Duplan J. *see* Novick, Reid, & others. 1991;51:853–9,CV
Duran C. Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair. 1991;51:972,IC
Duran CMG. *see* Balasundaram, Vega, & others. 1991;51:506–7,HW
Duran C. *see* Balasundaram & Duran. 1991;51:1046,CP
Dyadyurko AM. *see* Bockeria, Kupatadze, & others. 1991;51:563–72*
Dzik WH. *see* Shahian & Dzik. 1991;51:835–6,IC

Eales F. *see* Emery, Eales, & others. 1991;51:43–7*
Eastridge CE, Mahfood SS, Walker WA, Cole FH Jr. Delayed chest wall pain due to sternal wire sutures. 1991;51:56–9*
Eddy AC. *see* Allen, Slachman, & others. 1991;51:593–8*
Edmunds LH Jr. Uncomfortable issues. Reply. 1991;51:347–8,CP
Edwards FH. *see* Cohen, Thompson, & others. 1991;51:378–86*
Edwards NM. *see* Sanchez, Marboe, & others. 1991;51:30–3*
Edwards R. *see* Holman, Smith, & others. 1991;51:833–6,CR
Egan TM. *see* Lambert, Egan, & others. 1991;51:924–30*
Egawa Y. *see* Kitagawa, Katoh, & others. 1991;51:680–2,HW
Egrie JC. *see* Levine, Rosen, & others. 1991;51:764–6*
Eijsman L. *see* Harder, Eijsman, & others. 1991;51:936–41*
Ekroth R. *see* Svedjeholm, Hallhagen, & others. 1991;51:262–70*
Elliott MJ. Early restenosis after extended end-to-end anastomosis at neonatal age. Reply. 1991;51:162,CP
Elliott MJ. *see* Howell, Ho, & others. 1991;51:394–400*
Elliott MJ. *see* Snir, de Leval, & others. 1991;51:979–82*
Emery RW, Eales F, Joyce LD, Von Rueden TJ, King RM, Jorgensen CR, Pritzker MR, Johnson KE, Lake KD, Arom KV. Mechanical circulatory assistance after heart transplantation. 1991;51:43–7*
Eng J, Ravichandran PS, Kay PH, Murday AJ. Long-term results of Ionescu-Shiley valve in the tricuspid position. 1991;51:200–3*
Eng J, Sabanathan S. Site of action of continuous extrapleural intercostal nerve block. 1991;51:387–9*
Eng J, Sabanathan S. Airway complications in relapsing polychondritis. 1991;51:686–92,CT
Engelman RM. Retrograde continuous warm blood cardioplegia. 1991;51:180–1,ED
Enghoff EH. *see* Henze, Thorelius, & others. 1991;51:125–7,CR
Ercan H. *see* Berreklouw, Ercan, & others. 1991;51:293–5*
Esposito G. *see* Di Eusanio, Mazzola, & others. 1991;51:131–2,CR
Even P. *see* Meyer, Tamisier, & others. 1991;51:232–6*
Everson CT. *see* Mills & Everson. 1991;51:208–14*

Faling LJ. *see* Daly, Faling, & others. 1991;51:465–9*
Fareed J. *see* Walenga, Bakhos, & others. 1991;51:271–7*
Fedderson B. *see* Boldt, Zickmann, & others. 1991;51:747–53*
Feilberg VL. *see* Campanella, Cameron, & others. 1991;51:1046,CP
Felipe HS. *see* Assad, Felipe, & others. 1991;51:678–9,HW
Fellows D. *see* Meade, Moad, & others. 1991;51:488–90,CR
Feng WC, Singh AK. Management of endobronchial hemorrhage. 1991;51:1045–6,CP

Ferguson MK. Evolution of therapy for pharyngoesophageal (Zenker's) diverticulum. 1991;51:848–52,CL

Ferguson TB. Wanderjahr: The education of a surgeon, Edward D. Churchill, edited and annotated by J. Gordon Scannell. 1991;51:968,RV

Ferguson TB Jr, Cox JL. Temporary external DDD pacing after cardiac operations. 1991;51:723–32*

Fernandez J. *see* Adkins, Laub, & others. 1991;51:476–8,CR

Fernandez J. *see* Shapira, Fernandez, & others. 1991;51:969–72*

Fetherston GJ, Davis BB. Surgical management of carcinoid heart disease. 1991;51:493–4,CR

Fiasse RH. *see* Collard, Koninck, & others. 1991;51:34–8*

Finch EL. Anesthesia for cardiac surgery, by James A. DiNardo and Michael J. Schwartz. 1991;51:763,RV

Finck SJ. *see* Wolfe, Finck, & others. 1991;51:116–8,CR

Fiore AC. *see* Naunheim, Kesler, & others. 1991;51:547–51*

Fischer M. *see* Browdie, Bernstein, & others. 1991;51:290–2*

Fitzgerald D. *see* Skillington, Couper, & others. 1991;51:658–60,CR

Flanagan T. *see* Agee, Flanagan, & others. 1991;51:911–5*

Fleisher AG, McElvaney G, Robinson CLN. Multiple primary bronchogenic carcinomas: treatment and follow-up. 1991;51:48–51*

Flicker S. *see* Werthman, Sutter, & others. 1991;51:664–6,CR

Floten HS. *see* Palac, Strausbaugh, & others. 1991;51:479–81,CR

Follette DM. Penetrating cardiac injuries—a look to the future. 1991;51:701–2,ED

Forrester-Wood C. *see* Olak, Jeyasingham, & others. 1991;51:956–8*

Fosburg RG. Pleural diseases, second edition, by Richard W. Light, MD. 1991;51:663,RV

Frank G. *see* Heinemann, Frank, & others. 1991;51:827–8,CR

Frazier OH. *see* Putnam, Sweeney, & others. 1991;51:906–10*

Fremes SE. *see* Bloom, Goldman, & others. 1991;51:526,CP

Fremes SE. *see* Salerno, Christakis, & others. 1991;51:1023–5,HW

Freund PR. *see* Rusch, Freund, & others. 1991;51:323–4,HW

Friehs G. *see* Juettner, Arian-Schad, & others. 1991;51:302–3,CR

Frola C. *see* Ratto, Piacenza, & others. 1991;51:182–8*

Fujii K. *see* Nakasaki, Sugihara, & others. 1991;51:23–9*

Fujino S. *see* Yasuda, Mori, & others. 1991;51:242–4*

Fujiwara H. *see* Sharma, Fujiwara, & others. 1991;51:1031–9,CV

Fujiwara T. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR

Fukuchi S. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR

Fukuda S. *see* Takayama, Wanibuchi, & others. 1991;51:140–3,HW

Fullerton DA, Campbell DN, Whitman GJR. Use of human recombinant erythropoietin to correct severe preoperative anemia. 1991;51:825–6,CR

Furuta S. *see* Takayama, Wanibuchi, & others. 1991;51:140–3,HW

Fuse K. *see* Watanabe, Fuse, & others. 1991;51:767–72*

Fyfe DA. *see* Douville, Sade, & others. 1991;51:893–900*

Galbut D. *see* He, Hughes, & others. 1991;51:916–23,DI

Gale ME. *see* Daly, Faling, & others. 1991;51:465–9*

Gallagher JF. *see* Sutter, Goldman, & others. 1991;51:136–7,HW

Gallagher KP. *see* Bove & Gallagher. 1991;51:1044,CP

Gallhofer G. *see* Juettner, Arian-Schad, & others. 1991;51:302–3,CR

Galloway AC. *see* Grossi, Colvin, & others. 1991;51:484–7,CR

Gallucci V. *see* Bortolotti, Milano, & others. 1991;51:430–7*

Gallucci V. *see* Livi, Bortolotti, & others. 1991;51:524–5,CP

Galvin IF. Mammary artery grafts: a new no-touch technique for anastomosis. 1991;51:500–3,HW

Galvin IF, Black IW, Lee CL, Horton DA. Transesophageal echocardiography in acute aortic transection. 1991;51:310–1,CR

Ganzel BL. *see* Greene, Gray, & others. 1991;51:194–9*

Gao XD. *see* Gu, Wang, & others. 1991;51:573–8*

Gardner TJ. *see* Agee, Flanagan, & others. 1991;51:911–5,DI

Gardner TJ. *see* Brown, Holland, & others. 1991;51:359–67,DI

Gardner TJ. *see* Douville, Sade, & others. 1991;51:893–900,DI

Garwood A. *see* Sutter, Goldman, & others. 1991;51:136–7,HW

Gaskill HV III. Current practice of surgical stapling, edited by Mark M. Ravitch, Felicien M. Steichen, and Roger Welter. 1991;51:824,RV

Gaudiani VA, Mason HDW. Preoperative erythropoietin in Jehovah's Witnesses who require cardiac procedures. 1991;51:823–4,CR

Gaynes R, Bizek B, Mowry-Hanley J, Kirsh M. Risk factors for nosocomial pneumonia after coronary artery bypass graft operations. 1991;51:215–8*

Geffin GA. *see* Steinberg, Doherty, & others. 1991;51:620–9*

Geha A. *see* Goodnough & Geha. 1991;51:703–4,ED

Genco CM. *see* Breckwoldt, Genco, & others. 1991;51:959–63*

Gerosa G, McKay R, Ross DN. Replacement of the aortic valve or root with a pulmonary autograft in children. 1991;51:424–9*

Gertz SD. *see* Roberts, McIntosh, & others. 1991;51:455–60*

Ghidoni I. *see* Merlo, De Tommasi, & others. 1991;51:227–31*

Ghosh PK. Coronary ostial reconstruction: technical issues. 1991;51:673–5,HW

Giua R. *see* Ratto, Piacenza, & others. 1991;51:182–8*

Glass BA. *see* Paone, Mercer, & others. 1991;51:1010–1,CR

Gleason MM. *see* Arenas, Myers, & others. 1991;51:413–7*

Gold JP. Metallic surgical clips and magnetic resonance imaging. Reply. 1991;51:162–3,CP

Goldman BS. *see* Bloom, Goldman, & others. 1991;51:526,CP

Goldman SM. *see* Sutter, Goldman, & others. 1991;51:136–7,HW

Goldman SM. *see* Werthman, Sutter, & others. 1991;51:664–6,CR

Goldman S. *see* Sethi, Copeland, & others. 1991;51:733–8*

Goldstraw P. Staging lung cancer with computed tomography. 1991;51:345,CP

Goldstraw P. *see* Roxburgh, Thompson, & others. 1991;51:800–3*

Goodnough LT, Geha A. A new era in blood conservation. 1991;51:703–4,ED

Gordon D. *see* McKeown, Tsuboi, & others. 1991;51:636–41*

Gorton ME, Soltanzadeh H. Easy removal of surgically placed intraaortic balloon pump catheter. 1991;51:325–6,HW

Gotsman MS. *see* Mosseri, Meir, & others. 1991;51:248–52*

Gouge TH. *see* Guth, Gouge, & others. 1991;51:837–9,CR

Gould SA. *see* Levine, Rosen, & others. 1991;51:764–6*

Graeber GM, Collins JJH Jr, DeShong JL, Murray GF. Are sutures better than staples for closing bronchi and pulmonary vessels? 1991;51:901–5*

Graham AL. *see* Abbott, Hill, & others. 1991;51:705–10,DI

Graham AL. *see* Stewart, Carey, & others. 1991;51:717–22,DI

Grande A. *see* Bex, Grande, & others. 1991;51:694–5,CP

Gray LA Jr. *see* Greene, Gray, & others. 1991;51:194–9*

Gray RJ. *see* Tsai, Nessim, & others. 1991;51:983–6*

Grecco O. *see* Rossi, Braile, & others. 1991;51:649–51,CR

Greene MA, Gray LA Jr, Slater AD, Ganzel BL, Mavroudis C. Emergency aortocoronary bypass after failed angioplasty. 1991;51:194–9*

Greenfield LJ. Misplaced caval filter and subsequent pericardial tamponade. 1991;51:301,IC

Gregorini R. *see* Di Eusanio, Mazzola, & others. 1991;51:131–2,CR

Grieco J. *see* Hinkamp, Sullivan, & others. 1991;51:1004–6,CR

Grillo HC. Dilemmas in cardiothoracic surgical education. 1991; 51:809–11,ED
Grillo HC. *see* Allen, Mathisen, & others. 1991;51:948–51*
Grillo HC. *see* Wilkins, Grillo, & others. 1991;51 888–92*
Grossi EA, Colvin SB, Galloway AC, Rutkowski M, Doyle EF, Crooke GA, Spencer FC. Repair of posterior left ventricular aneurysm in a six-year-old boy. 1991;51:484–7,CR
Grover FL. *see* Daly, Trastek, & others. 1991;51:368–77,DI
Grover FL. *see* Kon, Hines, & others. 1991;51:557–62,DI
Grover FL. *see* Lambert, Egan, & others. 1991;51:924–30,DI
Gu YJ, Wang YS, Chiang BY, Gao XD, Ye CX, Wildevuur CRH. Membrane oxygenator prevents lung reperfusion injury in canine cardiopulmonary bypass. 1991;51:573–8*
Guerra F. *see* Bortolotti, Milano, & others. 1991;51:430–7*
Guiraudon GM. *see* Louagie, Guiraudon, & others. 1991;51: 616–9*
Gumbs RV, Peniston RL, Nabhani HA, Henry LJ. Rib fractures complicating median sternotomy. 1991;51:952–5*
Guojin L. *see* Awad, Deslauriers, & others. 1991;51:534–40*
Gustafson R. *see* Abbott, Hill, & others. 1991;51 705–10*
Guth AA, Gouge TH, Depan HJ. Blast injury to the thoracic esophagus. 1991;51:837–9,CR
Guttmann RD. *see* Shennib, Nguyen, & others. 1991;51:630–5*
Guvendik L. *see* Millner, Guvendik, & others. 1991;51:831–2,CR
Guyton SW. Thoracic surgery, edited by H. Pichelmaier and F. W. Schildberg. 1991;51:955,RV

Haan C, Lazar HL, Bernard S, Rivers S, Zallnick J, Shemin RJ. Superiority of retrograde cardioplegia after acute coronary occlusion. 1991;51:408–12*
Hachida M, Nakano H, Hirai M; Shi CY. Percutaneous transaortic closure of postinfarctional ventricular septal rupture. 1991;51:655–7,CR
Haller A. *see* Cohen, Thompson, & others. 1991;51:378–86,DI.
Hallhagen S. *see* Svedjeholm, Hallhagen, & others. 1991;51:262–70*
Hallman GL. *see* Sharma, Fujiwara, & others. 1991;51:1031–9,CV
Hamanaka Y. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
Hamilton JRL, Brooks SG, Walker DR. Alternative technique for repair of sinus venosus atrial septal defect. 1991;51:144–6,HW
Hankins JR. *see* Attar, Suter, & others. 1991;51:711–7*
Harder MP, Eijsman L, Roozendaal KJ, van Oeveren W, Wildevuur CRH. Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass. 1991;51:936–41*
Harr CD. *see* Kon, Hines, & others. 1991;51:557–62*
Harrah JD. *see* Putnam, Sweeney, & others. 1991;51:906–10,DI
Hartz RS. Excimer laser angioplasty during aortocoronary bypass grafting. 1991;51:672,IC
Hasin Y. *see* Mosseri, Meir, & others. 1991;51:248–52*
Hayashi T. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR
Hayashi Y. *see* Watanabe, Shimizu, & others. 1991;51 253–61*
Hays T. *see* Schroeder, Albert, & others. 1991;51:491–2,CR
Hayward RH, Korompai FL, Knight WL. Long-term follow-up of the Vineberg internal mammary artery implant procedure. 1991;51:1002–3,CR
Hazelrigg SR. *see* Landreneau, Hazelrigg, & others. 1991;51: 973–8*
Hazelrigg SR. *see* Landreneau, Hinson, & others. 1991;51:473–5,CR
Hazelrigg SR. *see* Landreneau, Marshall, & others. 1991;51:128–30,CR
He G-W, Hughes CF, McCaughan B, Thomson DS, Leckie BD, Yang C-Q, Baird DK. Mitral valve replacement combined with coronary artery operation: determinants of early and late results. 1991;51:916–23*
Heath BJ. Mitral valve suture techniques. Reply. 1991;51:865–6,CP
Heath BJ. *see* Chambers & Heath. 1991;51:60–4*
Heinemann M, Frank G, Oldhafer KJ, Schmoll E. Infected intravenous port device causing tricuspid valve regurgitation. 1991;51:827–8,CR
Hempelmann G. *see* Boldt, Zickmann, & others. 1991;51:610–5*
Hempelmann G. *see* Boldt, Zickmann, & others. 1991;51:747–53*
Henderson W. *see* Sethi, Copeland, & others. 1991;51:733–8*
Henry LJ. *see* Gumbs, Peniston, & others. 1991;51:952–5*
Henze AC, Thorelius JB, Borowiec JW, Enghoff EH, Thurén JB. Ascites after rupture of dissecting aortic aneurysm into the right atrium. 1991;51:125–7,CR
Herold C. *see* Boldt, Zickmann, & others. 1991;51:610–5*
Herold C. *see* Boldt, Zickmann, & others. 1991;51:747–53*
Hess J. *see* Bogers, Sreeram, & others. 1991;51:312–4,CR
Hicks GL Jr. *see* Boustany, Murphy, & others. 1991;51:1007–9,CR
Hilgenberg AD. *see* Allen, Mathisen, & others. 1991;51:948–51*
Hill R. *see* Abbott, Hill, & others. 1991;51:705–10*
Hines MH. *see* Kon, Hines, & others. 1991;51:557–62*
Hinkamp T, Sullivan H, Bakhos M, Grieco J, Pifarre R. Orthotopic cardiac transplantation in two patients with previous malignancy. 1991;51:1004–6,CR
Hinkamp TJ, Pifarre R, Bakhos M, Blakeman B. Combined myocardial revascularization and abdominal aortic aneurysm repair. 1991;51:470–2*
Hinson JM Jr. *see* Landreneau, Hinson, & others. 1991;51:473–5,CR
Hirai M. *see* Hachida, Nakano, & others. 1991;51:655–7,CR
Hiraiwa T, Hayashi T, Kaneda M, Sakai T, Namikawa S, Kusagawa M, Kusano I. Rupture of a benign mediastinal teratoma into the right pleural cavity. 1991;51:110–2,CR
Hirschfeld K. *see* Shapira, Fernandez, & others. 1991;51:969–72*
Ho SY. *see* Howell, Ho, & others. 1991;51:394–400*
Hoaglin DC. *see* Steinberg, Doherty, & others. 1991;51:620–9*
Hodge AJ. *see* Yadava, Hodge, & others. 1991;51:189–93*
Holland FW. *see* Brown, Holland, & others. 1991;51:359–67*
Holland FW. *see* Brown, Parenteau, & others. 1991;51:739–46*
Holman WL, Smith SH, Edwards R, Huang ST. Agglutination of blood cardioplegia by cold-reacting autoantibodies. 1991; 51:833–6,CR
Horowitz MD. *see* Attar, Suter, & others. 1991;51:711–7,DI
Horowitz MD. *see* Stewart, Carey, & others. 1991;51:717–22,DI
Horrigan TP. *see* Rosalion, Snow, & others. 1991;51:81–5*
Horton DA. *see* Galvin, Black, & others. 1991;51:310–1,CR
Houck JP. *see* Salerno, Houck, & others. 1991;51:245–7*
Houck J. *see* Salerno, Christakis, & others. 1991;51:1023–5,HW
Howe RW. *see* Jones, Rawitscher, & others. 1991;51:541–6,DI
Howell CE, Ho SY, Anderson RH, Elliott MJ. Fibrous skeleton and ventricular outflow tracts in double-outlet right ventricle. 1991;51:394–400*
Huang H-S. *see* Chang, Lin, & others. 1991;51:661–3,CR
Huang M-S. *see* Daly, Trastek, & others. 1991;51:368–77*
Huang ST. *see* Holman, Smith, & others. 1991;51:833–6,CR
Hughes CF. *see* He, Hughes, & others. 1991;51:916–23*
Hughes CF. *see* Korula & Hughes. 1991;51:667–9,CR
Huston C. *see* Copeland, Rosado, & others. 1991;51:1014–6,CR
Hutchins GM. *see* Boruchow & Hutchins. 1991;51:317–9,CR
Hutter J. *see* Olak, Jeyasingham, & others. 1991;51:956–8*

Iizuka T. *see* Kato, Watanabe, & others. 1991;51:931–5*
Ikawa S. *see* Kato, Nakada, & others. 1991;51:495–6,CR
Ikeda K. *see* Sato, Murakami, & others. 1991;51:754–8*

Imai Y, Kurosawa H, Fujiwara T, Fukuchi S, Matsuo K, Kawada M, Ohtsuka G. Palliative repair of aortic atresia associated with tricuspid atresia and transposition of the great arteries. 1991;51:646–8,CR
Ishida K. *see* Sato, Murakami, & others. 1991;51:754–8*
Ishihara H. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
Ishihara T. *see* Kato, Kobayashi, & others. 1991;51:327–9,HW
Iwa T. Epicardial and endocardial catheter ablation for Wolff-Parkinson-White syndrome. 1991;51:527–8,ED
Iwa T. *see* Watanabe, Shimizu, & others. 1991;51:253–61*
Iyer KS, Mee RBB. Staged repair of pulmonary atresia with ventricular septal defect and major systemic to pulmonary artery collaterals. 1991;51:65–72*

Jacob R. *see* Wilson, Lattner, & others. 1991;51:225–6*
Jacovoni P. *see* Ratto, Piacenza, & others. 1991;51:182–8*
Jatene AD. Jatene's arterial repair for transposition of the great vessels. 1991;51:513–4,IC
Jatene AD. *see* Assad, Felipe, & others. 1991;51:678–9,HW
Jatene AD. *see* Pêgo-Fernandes, Stolf, & others. 1991;51:438–42*
Jayanthi V. *see* Victor, Jayanthi, & others. 1991;51:522–3,CP
Jeevanandum V. *see* Sanchez, Marboe, & others. 1991;51:30–3*
Jeyasingham K. *see* Olak, Jeyasingham, & others. 1991;51:956–8*
Joachimsson PO. *see* Svedjeholm, Hallhagen, & others. 1991;51:262–70*
Johansson S. *see* Massa, Johansson, & others. 1991;51:94–101*
Johnson JA. *see* Landreneau, Hazelrigg, & others. 1991;51:973–8*
Johnson JA. *see* Landreneau, Hinson, & others. 1991;51:473–5,CR
Johnson JA. *see* Landreneau, Marshall, & others. 1991;51:128–30,CR
Johnson KE. *see* Emery, Eales, & others. 1991;51:43–7*
Johnsson P, Algotsson L, Ryding E, Ståhl E, Messeter K. Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease. 1991;51:579–84*
Johnston RH Jr. *see* Putnam, Sweeney, & others. 1991;51:906–10,DI
Jones JW, Rawitscher RE, McLean TR, Beall AC Jr, Thornby JI. Benefit from combining blood conservation measures in cardiac operations. 1991;51:541–6*
Jorgensen CR. *see* Emery, Eales, & others. 1991;51:43–7*
Joyce LD. *see* Emery, Eales, & others. 1991;51:43–7*
Judd DR. *see* Naunheim, Kesler, & others. 1991;51:547–51*
Juettner FM, Arian-Schad K, Kraus I, Gallhofer G, Popper H, Friehs G. Total unilateral lung gangrene in Hodgkin's disease: treatment by thoracostomy. 1991;51:302–3,CR
Juma A. *see* Parry & Juma. 1991;51:346,CP

Kaarela O. *see* Waris, Kaarela, & others. 1991;51:133–5,CR
Kabeer M. *see* Victor & Kabeer. 1991;51:345–6,CP
Kachaner J. *see* Serraf, Bruniaux, & others. 1991;51:1017–9,CR
Kaneda M. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR
Karchmer AW. *see* Lahey, Meyer, & others. 1991;51:299–301,CR
Karwande SV. *see* Morton, Karwande, & others. 1991;51:759–63*
Kass RM. *see* Tsai, Nessim, & others. 1991;51:983–6*
Kato H, Nakada T, Ikawa S, Miura T, Koh T, Tsuchitani Y. False aneurysm formation of the great arteries after arterial switch operation. 1991;51:495–6,CR
Kato H, Watanabe H, Tachimori Y, Iizuka T. Evaluation of neck lymph node dissection for thoracic esophageal carcinoma. 1991;51:931–5*
Kato H. *see* Yasuda, Mori, & others. 1991;51:242–4*
Kato R, Kobayashi T, Watanabe M, Kawamura M, Kikuchi K, Kobayashi K, Ishihara T. Improved technique for inserting a T tube in patients with subglottic stenosis. 1991;51:327–9,HW
Katoh I. *see* Kitagawa, Katoh, & others. 1991;51:680–2,HW
Katz D. *see* Crittenden, Roberts, & others. 1991;51:942–7*
Kawada M. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR
Kawamura M. *see* Kato, Kobayashi, & others. 1991;51:327–9,HW
Kay PH. *see* Eng, Ravichandran, & others. 1991;51:200–3*
Kayali MT. *see* Raffa, Mosieri, & others. 1991;51:996–8,CR
Keagy BA. *see* Lambert, Egan, & others. 1991;51:924–30*
Kerr AR. *see* Calder, Chan, & others. 1991;51:401–7*
Kesler KA. *see* Naunheim, Kesler, & others. 1991;51:547–51*
Kestens PJ. *see* Collard, Koninck, & others. 1991;51:34–8*
Khan SS. *see* Tsai, Nessim, & others. 1991;51:983–6*
Kiernan ME. *see* Ponn, Blancaflor, & others. 1991;51:605–9*
Kikuchi K. *see* Kato, Kobayashi, & others. 1991;51:327–9,HW
Kikui M. *see* Okumura, Ohshima, & others. 1991;51:599–604*
Kimblad P-O. *see* Massa, Johansson, & others. 1991;51:94–101*
King RM. *see* Emery, Eales, & others. 1991;51:43–7*
King S. *see* Sutter, Goldman, & others. 1991;51:136–7,HW
Kinney TB, Daily PO, Pfeffer TA. Optimizing myocardial hypothermia: I. Temperature probe design and clinical inferences. 1991;51:278–83*
Kinney TB. *see* Daily & Kinney. 1991;51:284–9*
Kirklin JK. Christiaan Barnard's contribution to the surgical treatment of Ebstein's malformation. 1991;51:147–51,CL
Kirklin JK. Prospects for understanding and eliminating the deleterious effects of cardiopulmonary bypass. 1991;51:529–31,ED
Kirklin JW. Training for cardiac surgery in children and adults. 1991;51:812–3,ED
Kirschner PA. *see* Wilkins, Grillo, & others. 1991;51:888–92,DI
Kirsh MM. *see* Putnam, Bolling, & others. 1991;51:482–3,CR
Kirsh M. *see* Gaynes, Bizek, & others. 1991;51:215–8*
Kitagawa T, Katoh I, Taki H, Wakisaka Y, Egawa Y, Takahashi Y, Akita H, Matsuoka S. New operative method for distal aortopulmonary septal defect. 1991;51:680–2,HW
Klein GJ. *see* Louagie, Guiraudon, & others. 1991;51:616–9*
Knight WL. *see* Hayward, Korompai, & others. 1991;51:1002–3,CR
Kobayashi K. *see* Kato, Kobayashi, & others. 1991;51:327–9,HW
Kobayashi T. *see* Kato, Kobayashi, & others. 1991;51:327–9,HW
Kobayasi T. *see* Watanabe, Fuse, & others. 1991;51:767–72*
Koch MO. *see* Stewart, Carey, & others. 1991;51:717–22*
Koh T. *see* Kato, Nakada, & others. 1991;51:495–6,CR
Koike R, Suma H. Pharmacological response of internal mammary artery and gastroepiploic artery. Reply. 1991;51:864–5,CP
Kon ND, Hines MH, Harr CD, Miller LR, Taylor CL, Cordell AR, Mills SA. Improved lung preservation with cold air storage. 1991;51:557–62*
Koninck XJD. *see* Collard, Koninck, & others. 1991;51:34–8*
Konishi H. *see* Watanabe, Fuse, & others. 1991;51:767–72*
Konishi T. *see* Watanabe, Fuse, & others. 1991;51:767–72*
Koolen JJ. *see* Moulijn, Smulders, & others. 1991;51:346,CP
Korompai FL. *see* Hayward, Korompai, & others. 1991;51:1002–3,CR
Korula R, Hughes CF. Squamous cell carcinoma arising in a sternotomy scar. 1991;51:667–9,CR
Kostuk WJ. *see* Novick, Menkis, & others. 1991;51:642–5*
Kotake Y. *see* Okumura, Ohshima, & others. 1991;51:599–604*
Kotliar C, Smart FW, Sekela ME, Pacifico A, Pratt CM, Noon GP, DeBakey ME, Young JB. Heterotopic heart transplantation and native heart ventricular arrhythmias. 1991;51:987–91*
Kouchoukos NT. *see* Wareing & Kouchoukos. 1991;51:443–7*
Koul B, Willen H, Sjöberg T, Wetterberg T, Kugelberg J, Steen S. Pulmonary sequelae of prolonged total venoarterial by-

pass: evaluation with a new experimental model. 1991;51:794–9*
Kratz JM. *see* Ferguson & Cox. 1991;51:723–32,DI
Kratz JM. *see* Reed, Marsh, & others. 1991;51:552–6*
Kratz JM. *see* Sethi, Copeland, & others. 1991;51:733–8,DI
Kraus I. *see* Juettner, Arian-Schad, & others. 1991;51:302–3,CR
Kriett JM. Heart and heart-lung transplantation, by William A. Baumgartner, Bruce A. Reitz, and S. C. Achuff. 1991;51:572,RV
Kron IL. Gastrotracheal fistula as a result of radiotherapy after transhiatal esophagectomy. Reply. 1991;51:697,CP
Kron IL. Risk of reintervention after coarctation repair. Reply. 1991;51:2,CP
Kron IL. *see* Agee, Flanagan, & others. 1991;51:911–5*
Kugelberg J. *see* Koul, Willen, & others. 1991;51:794–9*
Kuo T-T. *see* Chang, Lin, & others. 1991;51:661–3,CR
Kupatadze NI. *see* Bockeria, Kupatadze, & others. 1991;51:563–72*
Kurlansky PA. *see* Jones, Rawitscher, & others. 1991;51:541–6,DI
Kurosawa H. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR
Kusagawa M. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR
Kusano I. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR

Lacour-Gayet F. *see* Serraf, Bruniaux, & others. 1991;51:1017–9,CR
Lacquet LK. *see* van Son, Daniëls, & others. 1991;51:344,CP
Lacquet LK. *see* van Son & Lacquet. 1991;51:521,CP
Lacquet LK. *see* van Son, Smedts, & others. 1991;51:160–2,CP
Lahey SJ, Meyer LP, Karchmer AW, Cronin J, Czorniak M, Maggs PR, Nesto RW. Misplaced caval filter and subsequent pericardial tamponade. 1991;51:299–301,CR
Lake KD. *see* Emery, Eales, & others. 1991;51:43–7*
Laks H. *see* Capouya & Laks. 1991;51:860–3,KR
Lambert CJ Jr, Egan TM, Detterbeck FC, Keagy BA, Wilcox BR. Enhanced pulmonary function using dimethylthiourea for twelve-hour lung preservation. 1991;51:924–30*
Lambert CJ. *see* He, Hughes, & others. 1991;51:916–23,DI
Lambert CJ. *see* Jones, Rawitscher, & others. 1991;51:541–6,DI
Lamberti JJ. Palliation of univentricular heart without increasing ventricular work. 1991;51:882–3,ED
Landreneau RJ, Hazelrigg SR, Johnson JA, Boley TM, Nawaraworg W, Curtis JJ. Neodymium:yttrium-aluminum garnet laser–assisted pulmonary resections. 1991;51:973–8*
Landreneau RJ, Hinson JM Jr, Hazelrigg SR, Johnson JA, Boley TM, Curtis JJ. Strut fixation of an extensive flail chest. 1991;51:473–5,CR
Landreneau RJ, Marshall JB, McClelland RN, Curtis JJ, Johnson JA, Hazelrigg SR. New surgical approach to complicated gastroesophageal reflux disease: transthoracic parietal cell vagotomy. 1991;51:128–30,CR
Lanza LA, Putnam JB Jr, Benjamin RS, Roth JA. Response to chemotherapy does not predict survival after resection of sarcomatous pulmonary metastases. 1991;51:219–24*
Lanza LA. *see* Putnam, Sweeney, & others. 1991;51:906–10*
Lattner S. *see* Wilson, Lattner, & others. 1991;51 225–6*
Laub GW. *see* Adkins, Laub, & others. 1991;51:476–8,CR
Lazar HL. *see* Haan, Lazar, & others. 1991;51:408–12*
Le Dref O. *see* Menasché, Subayi, & others. 1991;51:418–23*
Lebidois J. *see* Serraf, Bruniaux, & others. 1991;51:1017–9,CR
Leca F. *see* Meyer, Tamisier, & others. 1991;51:232–6*
Leckie BD. *see* He, Hughes, & others. 1991;51:916–23*
Lee CL. *see* Galvin, Black, & others. 1991;51:310–1,CR
Lee M-C, Wong S-S, Chu J-J, Chang J-P, Lin P-J, Shieh M-J, Chang C-H. Traumatic asphyxia. 1991;51:86–8*
Lee M-C. *see* Chang, Lin, & others. 1991;51:661–3,CR
Lee RW. *see* Copeland, Rosado, & others. 1991;51:1014–6,CR
Lee SM. *see* Coltharp, Lee, & others. 1991;51:308–9,CR
Lee S-T. *see* Lee, Lee, & others. 1991;51:1020–2,HW
Lee Y-C, Lee S-T, Chu S-H. New technique of esophageal exclusion for chronic esophageal perforation. 1991;51:1020–2,HW
Lemmer JH Jr. Mitral valve suture techniques. 1991;51:865,CP
Lemole GM. *see* Shapira, Fernandez, & others. 1991;51:969–72*
Lessana A. *see* Noera, Sanguinetti, & others. 1991;51:320–2,CR
Levine EA, Rosen AL, Sehgal LR, Gould SA, Egrie JC, Moss GS. Erythropoietin deficiency after coronary artery bypass procedures. 1991;51:764–6*
Levine SM. Diagnosis of diseases of the chest, vol 4, 3rd edition, by Robert B. Fraser, J. A. Peter Pare, P. D. Pare, Richard S. Fraser, and George P. Genereux. 1991;51:1016,RV
Levitsky S. *see* Novitzky, Matthews, & others. 1991;51:10–7,DI
Levitsky S. *see* Ting, Silverman, & others. 1991;51:18–22*
Lewis CTP, Murphy MC, Cooley DA. Risk factors for cardiac operations in adult Jehovah's Witnesses. 1991;51:448–50*
Lewis JW Jr. Staging lung cancer with computed tomography. Reply. 1991;51:345,CP
Leyro-Diaz RM. *see* Scovotti, Ponzone, & others. 1991;51:844–5,HW
Libby JA. *see* Cilley, Cernaianu, & others. 1991;51:504–5,HW
Lichtenstein SV. *see* Salerno, Christakis, & others. 1991;51:1023–5,HW
Lichtenstein SV. *see* Salerno, Houck, & others. 1991;51:245–7*
Lin PJ. *see* Chang, Lin, & others. 1991;51:661–3,CR
Lin P-J. *see* Lee, Wong, & others. 1991;51:86–8*
Lin PJ. *see* Pearson, Lin, & others. 1991;51:788–93*
Livi U, Bortolotti U, Gallucci V. Inverted internal mammary artery for myocardial revascularization. 1991;51:524–5,CP
Lloyd L. *see* Lochner, Lloyd, & others. 1991;51:777–87*
Lochner A, Lloyd L, Brits W, Coetzee A. Oxygenation of cardioplegic solutions: a note of caution. 1991;51:777–87*
Lockhart CG. *see* Daly, Trastek, & others. 1991;51:368–77,DI
Lodi R. *see* Noera, Sanguinetti, & others. 1991;51:320–2,CR
Lotan C. *see* Mosseri, Meir, & others. 1991;51:248–52*
Louagie YAG, Guiraudon GM, Klein GJ, Yee R. Closed heart cryoablation of the His bundle using an anterior septal approach. 1991;51:616–9*
Lupinetti FM. *see* Christy, Lupinetti, & others. 1991;51:204–7*
Lynch RE. *see* Morton, Karwande, & others. 1991;51:759–63*
Lytle BW. Heart and brain, brain and heart, edited by Prof Dr(Med) Helge Refsum, Prof Dr(Med) Ilmar A. Sulg, and Prof Dr(Med) Knut Rasmussen. 1991;51:666,RV

Maat L, van Herwerden LA, van den Brand M, Bos E. An unusual problem during surgical removal of a broken guidewire. 1991;51:829–30,CR
MacIntosh EL, Parrott JCW, Unruh HW. Fistulas between the aorta and tracheobronchial tree. 1991;51:515–9,CT
Madanagopalan N. *see* Victor, Jayanthi, & others. 1991;51:522–3,CP
Maggi G, Casadio C, Cavallo A, Cianci R, Molinatti M, Ruffini E. Thymoma: results of 241 operated cases. 1991;51:152–6,CV
Maggs PR. *see* Lahey, Meyer, & others. 1991;51:299–301,CR
Mahfood SS. *see* Eastridge, Mahfood, & others. 1991;51:56–9*
Major D. *see* Awad, Deslauriers, & others. 1991;51:534–40*
Makowski S. *see* Meyer, Tamisier, & others. 1991;51:232–6*
Malcolm I. *see* Stubington & Malcolm. 1991;51:867,CP
Mamprin F. *see* Merlo, De Tommasi, & others. 1991;51:227–31*
Mankad PS, Chester AH, Yacoub MH. Role of potassium concentration in cardioplegic solutions in mediating endothelial damage. 1991;51:89–93*

Manolas E. *see* Cochrane, Warren, & others. 1991;51:652–4,CR
Mansour KA. Malignant fibrous histiocytoma of the trachea. Reply. 1991;51:695,CP
Mansour KA. *see* Cohen, Thompson, & others. 1991;51:378–86,DI
Mansour KA. *see* Daly, Trastek, & others. 1991;51:368–77,DI
Mansour KA. *see* Graeber, Collins, & others. 1991;51:901–5,DI
Mansour KA. *see* Reed, Marsh, & others. 1991;51:552–6,DI
Marboe CC. *see* Sanchez, Marboe, & others. 1991;51:30–3*
Marcial MB. *see* Assad, Felipe, & others. 1991;51:678–9,HW
Mardan AH. *see* Christy, Lupinetti, & others. 1991;51:204–7*
Marsh WH. *see* Reed, Marsh, & others. 1991;51:552–6*
Marshall JB. *see* Landreneau, Marshall, & others. 1991;51:128–30,CR
Martin L. *see* Awad, Deslauriers, & others. 1991;51:534–40*
Mason HDW. *see* Gaudiani & Mason. 1991;51:823–4,CR
Massa G, Johansson S, Kimblad P-O, Sjöberg T, Steen S. Might free arterial grafts fail due to spasm? 1991;51:94–101*
Mathisen DJ. *see* Allen, Mathisen, & others. 1991;51:948–51*
Mathisen DJ. *see* Wilkins, Grillo, & others. 1991;51:888–92*
Matloff JM. *see* Blanche, Segalowitz, & others. 1991;51:670–2,CR
Matloff JM. *see* Tsai, Nessim, & others. 1991;51:983–6*
Matsuo K. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR
Matsuoka S. *see* Kitagawa, Katoh, & others. 1991;51:680–2,HW
Matsuura Y. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
Matthews N. *see* Novitzky, Matthews, & others. 1991;51:10–7*
Matz LR. *see* Yadava, Hodge, & others. 1991;51:189–93*
Mavroudis C. *see* Douville, Sade, & others. 1991;51:893–900,DI
Mavroudis C. *see* Greene, Gray, & others. 1991;51:194–9*
Mazzola A. *see* Di Eusanio, Mazzola, & others. 1991;51:131–2,CR
Mazzucco A. *see* Bortolotti, Milano, & others. 1991;51:430–7*
McBride LR. *see* Naunheim, Kesler, & others. 1991;51:547–51*
McCaughan B. *see* He, Hughes, & others. 1991;51:916–23*
McClelland RN. *see* Landreneau, Marshall, & others. 1991;51:128–30,CR
McCrory D, Craig B, O'Kane H. Traumatic mitral valve rupture in a child. 1991;51:821–2,CR
McDonald TJ Jr. *see* Swain, McDonald, & others. 1991;51:105–9*
McDougal WS. *see* Stewart, Carey, & others. 1991;51:717–22*
McElvaney G. *see* Fleisher, McElvaney, & others. 1991;51:48–51*
McElvein RB. Neodymium:yttrium-aluminum garnet laser–assisted pulmonary resections. 1991;51:973–8,IC
McElvein RB. *see* Naunheim, Kesler, & others. 1991;51:547–51,DI
McElvein RB. *see* Reed, Marsh, & others. 1991;51:552–6,DI
McGrath LB. *see* Adkins, Laub, & others. 1991;51:476–8,CR
McIntosh CL. Atrioventricular valve replacement with a Hancock porcine xenograft. 1991;51:684,IC
McIntosh CL. *see* Brown, Roberts, & others. 1991;51:585–92*
McIntosh CL. *see* Roberts, McIntosh, & others. 1991;51:455–60*
McKay AM. *see* Bolling, Putnam, & others. 1991;51:52–5*
McKay R. *see* Gerosa, McKay, & others. 1991;51:424–9*
McKenzie FN. *see* Novick, Menkis, & others. 1991;51:642–5*
McKenzie FN. *see* Novick, Reid, & others. 1991;51:853–9,CV
McKeown PP, Tsuboi H, Togo T, Thomas R, Tuck R, Gordon D. Growth of tracheal anastomoses: advantage of absorbable interrupted sutures. 1991;51:636–41*
McLaughlin JS. *see* Attar, Suter, & others. 1991;51:711–7*
McLean TR, McManus RP. Penetrating trauma involving the innominate artery. 1991;51:113–5,CR
McLean TR. *see* Jones, Rawitscher, & others. 1991;51:541–6*
McManus RP. *see* McLean & McManus. 1991;51:113–5,CR
McNicholas KW. *see* Shapira, Fernandez, & others. 1991;51:969–72*
Meade P, Moad J, Fellows D, Adams CW. Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy. 1991;51:488–90,CR
Mee RBB. *see* Iyer & Mee. 1991;51:65–72*
Meir G. *see* Mosseri, Meir, & others. 1991;51:248–52*
Menasché P, Subayi J-B, Veyssié L, Le Dref O, Chevret S, Piwnica A. Efficacy of coronary sinus cardioplegia in patients with complete coronary artery occlusions. 1991;51:418–23*
Menkis AH. *see* Novick, Menkis, & others. 1991;51:642–5*
Menkis AH. *see* Novick, Reid, & others. 1991;51:853–9,CV
Mercer LC. *see* Paone, Mercer, & others. 1991;51:1010–1,CR
Merlo M, De Tommasi SM, Brunelli F, Abbruzzese PA, Crupi G, Ghidoni I, Casari A, Piti A, Mamprin F, Parenzan L. Long-term results after atrial correction of complete transposition of the great arteries. 1991;51:227–31*
Merrill WH. *see* Stewart, Carey, & others. 1991;51:717–22*
Messerschmidt WH. *see* Reed, Marsh, & others. 1991;51:552–6,DI
Messeter K. *see* Johnsson, Algotsson, & others. 1991;51:579–84*
Messmore HL. *see* Walenga, Bakhos, & others. 1991;51:271–7*
Mestres CA, Pomar JL, Acosta M, Ninot S, Barriuso C, Abad C, Mulet J. Delayed sternal closure for life-threatening complications in cardiac operations: an update. 1991;51:773–6*
Meyer G, Tamisier D, Sors H, Stern M, Vouhé P, Makowski S, Neveux J-Y, Leca F, Even P. Pulmonary embolectomy: a 20-year experience at one center. 1991;51:232–6*
Meyer LP. *see* Lahey, Meyer, & others. 1991;51:299–301,CR
Milano A. *see* Bortolotti, Milano, & others. 1991;51:430–7*
Miller LR. *see* Kon, Hines, & others. 1991;51:557–62*
Miller RF. *see* Coltharp, Lee, & others. 1991;51:308–9,CR
Millner RWJ, Guvendik L, Blauth C, Treasure T, Pepper JR. False aneurysm of the right internal mammary artery. 1991;51:831–2,CR
Mills NL, Everson CT. Technique for use of the inferior epigastric artery as a coronary bypass graft. 1991;51:208–14*
Mills SA. *see* Kon, Hines, & others. 1991;51:557–62*
Minemura T. *see* Takayama, Wanibuchi, & others. 1991;51:140–3,HW
Mitchell JM. *see* Sutter, Goldman, & others. 1991;51:136–7,HW
Mitomi T. *see* Nakasaki, Sugihara, & others. 1991;51:23–9*
Miura T. *see* Kato, Nakada, & others. 1991;51:495–6,CR
Moad J. *see* Meade, Moad, & others. 1991;51:488–90,CR
Molina JE. New technique for pacemaker implantation in the upper chest of children and women. 1991;51:992–5*
Molinatti M. *see* Maggi, Casadio, & others. 1991;51:152–6,CV
Moncure AC. *see* Allen, Mathisen, & others. 1991;51:948–51*
Moncure AC. *see* Wilkins, Grillo, & others. 1991;51:888–92*
Moreira LFP. *see* Pêgo-Fernandes, Stolf, & others. 1991;51:438–42*
Mori A. *see* Yasuda, Mori, & others. 1991;51:242–4*
Morino H. *see* Okumura, Ohshima, & others. 1991;51:599–604*
Moritz T. *see* Sethi, Copeland, & others. 1991;51:733–8*
Morton DL. *see* Colquhoun, Rosenthal, & others. 1991;51:390–3*
Morton KA, Karwande SV, Davis RK, Datz FL, Lynch RE. Gastric emptying after gastric interposition for cancer of the esophagus or hypopharynx. 1991;51:759–63*
Mosieri J. *see* Raffa, Mosieri, & others. 1991;51:996–8,CR
Moss GS. *see* Levine, Rosen, & others. 1991;51:764–6*
Mosseri M, Meir G, Lotan C, Hasin Y, Applebaum A, Rosenheck S, Shimon D, Gotsman MS. Coronary pathology predicts conduction disturbances after coronary artery bypass grafting. 1991;51:248–52*
Mossuto E. *see* Bortolotti, Milano, & others. 1991;51:430–7*
Mostow ND. *see* Rosalion, Snow, & others. 1991;51:81–5*
Moulijn AC, Smulders YM, Wiepking ME, Koolen JJ, van Wezel HB, Visser CA. Single drain (pleura, pericardium, mediastinum) after open heart operations. Reply. 1991;51:346,CP

Mowry-Hanley J. *see* Gaynes, Bizek, & others. 1991;51:215–8*
Mulder DG. *see* Dadourian, Perloff, & others. 1991;51:159–60,CP
Mulder DS. *see* Nguyen, Mulder, & others. 1991;51:76–80*
Mulder DS. *see* Shennib, Nguyen, & others. 1991;51:630–5*
Mulet J. *see* Mestres, Pomar, & others. 1991;51:773–6*
Mullerworth MH. *see* Smith, Mullerworth, & others. 1991;51:39–42*
Mullerworth M. *see* Cochrane, Warren, & others. 1991;51:652–4,CR
Munafo A. *see* Borgeat, Petropoulos, & others. 1991;51:964–8*
Munfakh NA. *see* Steinberg, Doherty, & others. 1991;51:620–9*
Murakami K. *see* Sato, Murakami, & others. 1991;51:754–8*
Murday AJ. *see* Eng, Ravichandran, & others. 1991;51:200–3*
Murphy GW. *see* Boustany, Murphy, & others. 1991;51:1007–9,CR
Murphy MC. *see* Lewis, Murphy, & others. 1991;51:443–50*
Murray GF. *see* Graeber, Collins, & others. 1991;51:901–5*
Murray G. *see* Abbott, Hill, & others. 1991;51:705–10*
Murtaugh PA. *see* Daly, Trastek, & others. 1991;51:368–77*
Musante F. *see* Ratto, Piacenza, & others. 1991;51:182–3*
Muskett AD. *see* Rosenbloom & Muskett. 1991;51:846–7,HW
Myers JL. *see* Arenas, Myers, & others. 1991;51:413–7*

Nabhani HA. *see* Gumbs, Peniston, & others. 1991;51:952–5*
Nakada T. *see* Kato, Nakada, & others. 1991;51:495–6,CR
Nakagawa H. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
Nakano H. *see* Hachida, Nakano, & others. 1991;51:655–7,CR
Nakasaki H, Sugihara T, Tajima T, Mitomi T, Osamura Y, Onoda N, Fujii K. Tracheoesophageal anastomosis for intractable aspiration pneumonia. 1991;51:23–9*
Namikawa S. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR
Nathan H. Nifedipine after coronary bypass grafting. 1991;51:693,CP
Naunheim KS, Kesler KA, D'Orazio SA, Fiore AC, McBride LR, Judd DR. Thoracotomy in the octogenarian. 1991;51:547–51*
Nawarawong W. *see* Landreneau, Hazelrigg, & others. 1991;51:973–8*
Nessim S. *see* Tsai, Nessim, & others. 1991;51:983–6*
Nesto RW. *see* Lahey, Meyer, & others. 1991;51:299–301,CR
Neutze JM. *see* Calder, Chan, & others. 1991;51:401–7*
Neveux J-Y. *see* Meyer, Tamisier, & others. 1991;51:232–6*
Nguyen DM, Mulder DS, Shennib H. Altered cellular immune function in the atelectatic lung. 1991;51:76–80*
Nguyen D. *see* Shennib & Nguyen. 1991;51:335–40,CV
Nguyen D. *see* Shennib, Nguyen, & others. 1991;51:630–5*
Ninot S. *see* Mestres, Pomar, & others. 1991;51:773–6*
Nissinen J. *see* Waris, Kaarela, & others. 1991;51:133–5,CR
Noera G, Sanguinetti M, Pensa P, Biagi B, Cremonesi A, Lodi R, Lessana A, Carbone C. Tricuspid valve incompetence caused by nonpenetrating thoracic trauma. 1991;51:320–2,CR
Noon DL. *see* Rosalion, Snow, & others. 1991;51:81–5*
Noon GP. *see* Kotliar, Smart, & others. 1991;51:987–91*
Noon GP. *see* Sekela, Verani, & others. 1991;51:804–6*
Norman AF. The first mitral valve replacement. 1991;51:525–6,CP
Novick RJ, Menkis AH, McKenzie FN, Reid KR, Pflugfelder PW, Kostuk WJ, Ahmad D. The safety of low-dose prednisone before and immediately after heart-lung transplantation. 1991;51:642–5*
Novick RJ, Reid KR, Denning L, Duplan J, Menkis AH, McKenzie FN. Prolonged preservation of canine lung allografts: the role of prostaglandins. 1991;51:853–9,CV
Novitzky D, Matthews N, Shawley D, Cooper DKC, Zuhdi N. Triiodothyronine in the recovery of stunned myocardium in dogs. 1991;51:10–7*

Ochsner JL. *see* Risher, Arensman, & others. 1991;51:346–7,CP
Oda M. *see* Watanabe, Shimizu, & others. 1991;51:253–61*
Ohshima S. *see* Okumura, Ohshima, & others. 1991;51:599–604*
Ohtsuka G. *see* Imai, Kurosawa, & others. 1991;51:646–8,CR
Okamoto M. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
O'Kane H. *see* McCrory, Craig, & others. 1991;51:821–2,CR
Okumura M, Ohshima S, Kotake Y, Morino H, Kikui M, Yasumitsu T. Intraoperative pleural lavage cytology in lung cancer patients. 1991;51:599–604*
Olak J, Jeyasingham K, Forrester-Wood C, Hutter J, Al-Zeerah M, Brown E. Randomized trial of one-dose versus six-dose cefazolin prophylaxis in elective general thoracic surgery. 1991;51:956–8*
Oldhafer KJ. *see* Heinemann, Frank, & others. 1991;51:827–8,CR
Olsen JB, Clemmensen O, Andersen K. Adenocarcinoma arising in a foregut cyst of the mediastinum. 1991;51:497–9,CR
Onoda N. *see* Nakasaki, Sugihara, & others. 1991;51:23–9*
Orringer MB. General thoracic surgery—issues and direction. 1991;51:814–7,ED
Osamura Y. *see* Nakasaki, Sugihara, & others. 1991;51:23–9*
Ott DA. *see* Sharma, Fujiwara, & others. 1991;51:1031–9,CV
Ott DA. *see* Trehan & Ott. 1991;51:122–4,CR
Otte JB. *see* Collard, Koninck, & others. 1991;51:34–8*
Otto CM. *see* Allen, Slachman, & others. 1991;51:593–8*

Paç M, Başoğlu A, Yediyildiz S, Yekeler I, Yilmaz A. Gastrotracheal fistula as a result of radiotherapy after transhiatal esophagectomy. 1991;51:696–7,CP
Paccagnella A, Simini G, Valfré C. Could glucose-insulin-potassium be considered only a step of a complete nutritional program for complicated cardiac patients? 1991;51:344,CP
Pacifico A. *see* Kotliar, Smart, & others. 1991;51:987–91*
Page CP. AIDS and surgery, edited by Andrew J. W. Sim and Donald J. Jefferies. 1991;51:836,RV
Pairolero PC, Trastek VF, Allen MS. Empyema and bronchopleural fistula. 1991;51:157–8,KR
Pairolero PC. *see* Daly, Trastek, & others. 1991;51:368–77*
Palac RT, Strausbaugh LJ, Antonovic R, Floten HS. An unusual complication of cardiac transplantation-infected aortic pseudoaneurysm. 1991;51:479–81,CR
Panos A. *see* Salerno, Houck, & others. 1991;51:245–7*
Paone RF, Mercer LC, Glass BA. Pneumonectomy secondary to *Mycobacterium fortuitum* in infancy. 1991;51:1010–1,CR
Parenteau GL. *see* Brown, Holland, & others. 1991;51:359–67*
Parenteau GL. *see* Brown, Parenteau, & others. 1991;51:739–46*
Parenzan L. *see* Merlo, De Tommasi, & others. 1991;51:227–31*
Parham JV. *see* Purut, Scott, & others. 1991;51:304–7,CR
Parrott JCW. *see* MacIntosh, Parrott, & others. 1991;51:515–9,CT
Parrott JCW. *see* Urschel & Parrott. 1991;51:1046,CP
Parry W, Juma A. Congenital bronchoesophageal fistula. 1991;51:346,CP
Pass HI. Symposium on thoracic surgical oncology. 1991;51:163,CP
Pass HI. *see* Agee, Flanagan, & others. 1991;51:911–5,DI
Pass HI. *see* Lambert, Egan, & others. 1991;51:924–30,DI
Pass HI. *see* Naunheim, Kesler, & others. 1991;51:547–51,DI
Pass HI. *see* Stewart, Carey, & others. 1991;51:717–22,DI
Pate JW. Penetrating trauma involving the innominate artery. 1991;51:114–5,IC
Pearlman AS. *see* Allen, Slachman, & others. 1991;51:593–8*

Pearson PJ, Lin PJ, Schaff HV. Production of endothelium-derived contracting factor is enhanced after coronary reperfusion. 1991;51:788–93*

Pêgo-Fernandes PM, Stolf NAG, Moreira LFP, Barreto ACP, Bittencourt D, Jatene AD. Management of aortic insufficiency in chronic aortic dissection. 1991;51:438–42*

Peigh PS, DiSesa VJ, Collins JJ Jr, Cohn LH. Coronary bypass grafting with totally calcified or acutely dissected ascending aorta. 1991;51:102–4*

Peigh PS. *see* Skillington, Couper, & others. 1991;51:658–60,CR

Pellett JR. *see* Chopra, Duke, & others. 1991;51:840–1,CR

Peniston RL. *see* Gumbs, Peniston, & others. 1991;51:952–5*

Penkoske PA. *see* Robertson, Penkoske, & others. 1991;51:73–5*

Pensa P. *see* Noera, Sanguinetti, & others. 1991;51:320–2,CR

Pepper JR. *see* Millner, Guvendik, & others. 1991;51:831–2,CR

Perloff JK. *see* Dadourian, Perloff, & others. 1991;51:159–60,CP

Perryman RA. Autogenous atrial tunnel for direct cavopulmonary connection in infants and small children. 1991;51:508–10,HW

Persellin ST. *see* Wolfe, Finck, & others. 1991;51:116–8,CR

Peters RM. Should we care? Do we care? What should we do? 1991;51:807–8,ED

Petropoulos P. *see* Borgeat, Petropoulos, & others. 1991;51:964–8*

Pfeffer TA. *see* Kinney, Daily, & others. 1991;51:278–83*

Pflugfelder PW. *see* Novick, Menkis, & others. 1991;51:642–5*

Piacenza G. *see* Ratto, Piacenza, & others. 1991;51:182–8*

Pifarré R. *see* Hinkamp, Sullivan, & others. 1991;51:1004–6,CR

Pifarre R. *see* Hinkamp, Pifarre, & others. 1991;51:470–2*

Pifarre R. *see* Walenga, Bakhos, & others. 1991;51:271–7*

Pinto GH. *see* Rossi, Braile, & others. 1991;51:649–51,CR

Pitì A. *see* Merlo, De Tommasi, & others. 1991;51:227–31*

Piwnica A. *see* Menasché, Subayi, & others. 1991;51:418–23*

Planche C. *see* Serraf, Bruniaux, & others. 1991;51:1017–9,CR

Pluth JR. The Starr valve revisited. 1991;51:333–4,CL

Pollock SB. *see* Adkins, Laub, & others. 1991;51:476–8,CR

Pomar JL. *see* Mestres, Pomar, & others. 1991;51:773–6*

Ponn RB, Blancaflor J, D'Agostino RS, Kiernan ME, Toole AL, Stern H. Pleuroperitoneal shunting for intractable pleural effusions. 1991;51:605–9*

Ponzone CA. *see* Scovotti, Ponzone, & others. 1991;51:844–5,HW

Poplavskaya LM. *see* Bockeria, Kupatadze, & others. 1991;51:563–72*

Popper H. *see* Juettner, Arian-Schad, & others. 1991;51:302–3,CR

Pratt CM. *see* Kotliar, Smart, & others. 1991;51:987–91*

Pritzker MR. *see* Emery, Eales, & others. 1991;51:43–7*

Puga FJ. Unifocalization for pulmonary atresia with ventricular septal defect. 1991;51:8–9,ED

Purut CM, Scott SM, Parham JV, Smith PK. Intraoperative management of severe endobronchial hemorrhage. 1991;51:304–7,CR

Putnam JB Jr, Bolling SF, Kirsh MM. Procainamide-induced respiratory insufficiency after cardiopulmonary bypass. 1991;51:482–3,CR

Putnam JB Jr, Sweeney MS, Colon R, Lanza LA, Frazier OH, Cooley DA. Primary cardiac sarcomas. 1991;51:906–10*

Putnam JB Jr. *see* Bolling, Putnam, & others. 1991;51:52–5*

Putnam JB Jr. *see* Lanza, Putnam, & others. 1991;51:219–24*

Quaegebeur JM. *see* Bogers, Sreeram, & others. 1991;51:312–4,CR

Raffa H, Mosieri J, Sorefan AA, Kayali MT. Sinus of Valsalva aneurysm eroding into the interventricular septum. 1991;51:996–8,CR

Rahko PS. *see* Chopra, Duke, & others. 1991;51:840–1,CR

Rainer WG. Profiles of leadership in thoracic surgery. 1991;51:877–81,PA

Ratto GB, Piacenza G, Frola C, Musante F, Serrano I, Giua R, Salio M, Jacovoni P, Rovida S. Chest wall involvement by lung cancer: computed tomographic detection and results of operation. 1991;51:182–8*

Ravichandran PS. *see* Eng, Ravichandran, & others. 1991;51:200–3*

Rawitscher RE. *see* Jones, Rawitscher, & others. 1991;51:541–6*

Rebelo LS. *see* Antunes, Vanderdonck, & others. 1991;51:999–1001,CR

Reed CE, Marsh WH, Carlson LS, Seymore CH, Kratz JM. Prospective, randomized trial of palliative treatment for unresectable cancer of the esophagus. 1991;51:552–6*

Reid KR. *see* Novick, Menkis, & others. 1991;51:642–5*

Reid KR. *see* Novick, Reid, & others. 1991;51:853–9,CV

Reul GJ. *see* Sharma, Fujiwara, & others. 1991;51:1031–9,CV

Ridley PD, Braimbridge MV. Thoracoscopic debridement and pleural irrigation in the management of empyema thoracis. 1991;51:461–4*

Risher WH, Arensman RM, Ochsner JL. Congenital bronchoesophageal fistula. Reply. 1991;51:346–7,CP

Rivers S. *see* Haan, Lazar, & others. 1991;51:408–12*

Robbins RC. *see* Swain, McDonald, & others. 1991;51:105–9*

Roberts CS, McIntosh CL, Brown PS Jr, Cannon RO III, Gertz SD, Clark RE. Reoperation for persistent outflow obstruction in hypertrophic cardiomyopathy. 1991;51:455–60*

Roberts CS. *see* Brown, Roberts, & others. 1991;51:585–92*

Roberts CS. *see* Crittenden, Roberts, & others. 1991;51:942–7*

Robertson JM. Ventricular perforation with valvoplasty. Reply. 1991;51:1043,CP

Robertson MA, Penkoske PA, Duncan NF. Right pulmonary artery obstruction after pulmonary artery banding. 1991;51:73–5*

Robicsek F. Apical aortic cannulation: application of an old method with new paraphernalia. 1991;51:330–2,HW

Robinson CLN. *see* Fleisher, McElvaney, & others. 1991;51:48–51*

Robinson LA. Calcium in neonatal cardioplegia. 1991;51:1043–4,CP

Roe BB. Lung cancer chronicles, by John A. Meyer, MD. 1991;51:654,RV

Ronquist G. *see* Svedjeholm, Hallhagen, & others. 1991;51:262–70*

Roozendaal KJ. *see* Harder, Eijsman, & others. 1991;51:936–41*

Rosa L. *see* Crittenden, Roberts, & others. 1991;51:942–7*

Rosado LJ. *see* Copeland, Rosado, & others. 1991;51:1014–6,CR

Rosalion A, Snow NJ, Horrigan TP, Noon DL, Mostow ND. Amiodarone versus bretylium for suppression of reperfusion arrhythmias in dogs. 1991;51:81–5*

Rose EA. *see* Sanchez, Marboe, & others. 1991;51:30–3*

Rosen AL. *see* Levine, Rosen, & others. 1991;51:764–6*

Rosenbloom M, Muskett AD. Simplified method for femoral venous cannulation. 1991;51:846–7,HW

Rosenheck S. *see* Mosseri, Meir, & others. 1991;51:248–52*

Rosenthal DL. *see* Colquhoun, Rosenthal, & others. 1991;51:390–3*

Ross DN. *see* Gerosa, McKay, & others. 1991;51:424–9*

Rossi MA, Braile DM, Souza DRS, Santos JLV, Thevenard RS, Pinto GH, Suzigan S, Grecco O. Dynamic cardiomyoplasty in chronic Chagas' heart disease: clinicopathological data. 1991;51:649–51,CR

Roth JA, Balch CM. Thoracic surgery training: it is time for a change. 1991;51:818–9,ED

Roth JA. *see* Lanza, Putnam, & others. 1991;51:219–24*

Rovida S. *see* Ratto, Piacenza, & others. 1991;51:182–8*

Roxburgh JC, Thompson J, Goldstraw P. Hospital mortality and long-term survival after pulmonary resection in the elderly. 1991;51:800–3*
Rudd RM. *see* Davies, Bailey, & others. 1991;51:695–6,CP
Ruffini E. *see* Maggi, Casadio, & others. 1991;51:152–6,CV
Rusch VW, Freund PR, Bowdle TA. Exchanging double-lumen for single-lumen endotracheal tubes after thoracotomy. 1991;51:323–4,HW
Rutkowski M. *see* Grossi, Colvin, & others. 1991;51:484–7,CR
Ryding E. *see* Johnsson, Algotsson, & others. 1991;51:579–84*

Sabanathan S. *see* Eng & Sabanathan. 1991;51:387–9*
Sabanathan S. *see* Eng & Sabanathan. 1991;51:686–92,CT
Sade RM. *see* Cohen, Thompson, & others. 1991;51:378–86,DI
Sade RM. *see* Douville, Sade, & others. 1991;51:893–900*
Sade RM. *see* Jones, Rawitscher, & others. 1991;51:541–6,DI
Safford RE. *see* Wolfe, Finck, & others. 1991;51:116–8,CR
Saito K. *see* Sato, Murakami, & others. 1991;51:754–8*
Saito T. *see* Takayama, Wanibuchi, & others. 1991;51:140–3,HW
Sakai T. *see* Hiraiwa, Hayashi, & others. 1991;51:110–2,CR
Salerno TA, Christakis GT, Abel J, Houck J, Barrozo CAM, Fremes SE, Cusimano RJ, Lichtenstein SV. Technique and pitfalls of retrograde continuous warm blood cardioplegia. 1991;51:1023–5,HW
Salerno TA, Houck JP, Barrozo CAM, Panos A, Christakis GT, Abel JG, Lichtenstein SV. Retrograde continuous warm blood cardioplegia: a new concept in myocardial protection. 1991;51:245–7*
Salerno TA. *see* Christakis & Salerno. 1991;51:53–4,IC
Salio M. *see* Ratto, Piacenza, & others. 1991;51:182–8*
Sanchez JA, Marboe CC, Auteri JS, Jeevanandum V, Edwards NM, Berger CL, Rose EA. Binding of preformed xenoantibodies to porcine bioprosthetic valves. 1991;51:30–3*
Sanguinetti M. *see* Noera, Sanguinetti, & others. 1991;51:320–2,CR
Santos GH. Late volume changes in retrosternal colon bypass. 1991;51:296–8,CR
Santos JLV. *see* Rossi, Braile, & others. 1991;51:649–51,CR
Saprigin DB. *see* Bockeria, Kupatadze, & others. 1991;51:563–72*
Sato N, Murakami K, Ishida K, Ikeda K, Saito K. Pulmonary hypertension and polymorphonuclear leukocyte elastase after esophageal cancer operations. 1991;51:754–8*
Scannell JG. *see* Wilkins, Grillo, & others. 1991;51:888–92*
Schaff HV. *see* Pearson, Lin, & others. 1991;51:788–93*
Schaffer M. *see* Schroeder, Albert, & others. 1991;51:491–2,CR
Schmoll E. *see* Heinemann, Frank, & others. 1991;51:827–8,CR
Schönberger JP. *see* Berreklouw, Ercan, & others. 1991;51:293–5*
Schroeder J, Albert J, Clarke D, Schaffer M, Wolfe R, Hays T. Hemolysis due to branch pulmonary stenosis after the arterial switch procedure. 1991;51:491–2,CR
Schwander D. *see* Borgeat, Petropoulos, & others. 1991;51:964–8*
Scott SM. *see* Purut, Scott, & others. 1991;51:304–7,CR
Scovotti CA, Ponzone CA, Leyro-Diaz RM. Reinforced sternal closure. 1991;51:844–5,HW
Segalowitz J. *see* Blanche, Segalowitz, & others. 1991;51:670–2,CR
Sehgal LR. *see* Levine, Rosen, & others. 1991;51:764–6*
Sekela ME, Verani MS, Noon GP. Comparison of hemodynamics and ejection fraction during left heart bypass. 1991;51:804–6*
Sekela ME. *see* Kotliar, Smart, & others. 1991;51:987–91*
Sequeira A. *see* Attar, Suter, & others. 1991;51:711–7*
Serra AJ. *see* Shapira, Fernandez, & others. 1991;51:969–72*
Serraf A, Bruniaux J, Lebidois J, Lacour-Gayet F, Kachaner J, Planche C. Aortic atresia with normal left ventricle. 1991;51:1017–9,CR
Serrano I. *see* Ratto, Piacenza, & others. 1991;51:182–8*
Sethi GK, Copeland JG, Moritz T, Henderson W, Zadina K, Goldman S. Comparison of postoperative complications between saphenous vein and IMA grafts to left anterior descending coronary artery. 1991;51:733–8*
Sethi G. *see* Copeland, Rosado, & others. 1991;51:1014–6,CR
Seymore CH. *see* Reed, Marsh, & others. 1991;51:552–6*
Shahian DM, Dzik WH. Agglutination of blood cardioplegia by cold-reacting autoantibodies. 1991;51:835–6,IC
Shapira N, Fernandez J, McNicholas KW, Serra AJ, Hirschfeld K, Spagna PM, Lemole GM. Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair. 1991;51:969–72*
Shapshay SM. *see* Streitz & Shapshay. 1991;51:695,CP
Sharma BK, Fujiwara H, Hallman GL, Ott DA, Reul GJ, Cooley DA. Supravalvar aortic stenosis: a 29-year review of surgical experience. 1991;51:1031–9,CV
Sharma VK. *see* Arsiwala, Bedi, & others. 1991;51:348,CP
Shawley D. *see* Novitzky, Matthews, & others. 1991;51:10–7*
Shears L. *see* Abbott, Hill, & others. 1991;51:705–10*
Shemin RJ. *see* Haan, Lazar, & others. 1991;51:408–12*
Shennib H, Nguyen D. Bronchoalveolar lavage in lung transplantation. 1991;51:335–40,CV
Shennib H, Nguyen D, Guttmann RD, Mulder DS. Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection. 1991;51:630–5*
Shennib H. *see* Nguyen, Mulder, & others. 1991;51:76–80*
Shennib H. *see* Ward, Shennib, & others. 1991;51:451–4*
Shi CY. *see* Hachida, Nakano, & others. 1991;51:655–7,CR
Shibata Y. *see* Watanabe, Fuse, & others. 1991;51:767–72*
Shieh M-J. *see* Chang, Lin, & others. 1991;51:661–3,CR
Shieh M-J. *see* Lee, Wong, & others. 1991;51:86–8*
Shikata H. *see* Sueda, Matsuura, & others. 1991;51:119–21,CR
Shimizu J. *see* Watanabe, Shimizu, & others. 1991;51:253–61*
Shimon D. *see* Mosseri, Meir, & others. 1991;51:248–52*
Siddiqui MAA. *see* Taggart, Siddiqui, & others. 1991;51:693–4,CP
Silverman NA. Mediastinal masses. 1991;51:520,KR
Silverman N. *see* Ting, Silverman, & others. 1991;51:18–22*
Simini G. *see* Paccagnella, Simini, & others. 1991;51:344,CP
Sindhi R, Belisle J, Cleveland RJ, Diehl JT. Patch aortotomy for aortic valve replacement after previous coronary artery bypass grafting. 1991;51:676–7,HW
Singh AK. *see* Feng & Singh. 1991;51:1045–6,CP
Sjöberg T. *see* Koul, Willen, & others. 1991;51:794–9*
Sjöberg T. *see* Massa, Johansson, & others. 1991;51:94–101*
Skillington PD, Couper GS, Peigh PS, Fitzgerald D, Cohn LH. Pulmonary artery balloon counterpulsation for intraoperative right ventricular failure. 1991;51:658–60,CR
Skinner DB. Cervical lymph node dissection for thoracic esophageal cancer. 1991;51:884–5,ED
Slachman F. *see* Allen, Slachman, & others. 1991;51:593–8*
Slater AD. *see* Greene, Gray, & others. 1991;51:194–9*
Smart FW. *see* Kotliar, Smart, & others. 1991;51:987–91*
Smedts F. *see* van Son & Smedts. 1991;51:864,CP
Smedts F. *see* van Son, Smedts, & others. 1991;51:160–2,CP
Smith JA, Mullerworth MH, Westlake GW, Tatoulis J. Empyema thoracis: 14-year experience in a teaching center. 1991;51:39–42*
Smith JHF. *see* Cooper, Boucher, & others. 1991;51:1012–3,CR
Smith PK. Ventricular perforation with valvoplasty. 1991;51:1042–3,CP
Smith PK. *see* Purut, Scott, & others. 1991;51:304–7,CR
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* = Original Article
AN = Announcement
CL = Classics in Thoracic Surgery
CR = Case Report
CP = Correspondence
CT = Collective Review
CV = Current Review
ED = Editorial
HW = How to Do It
KR = Key References
PA = Presidential Address
RE = Report
RV = Review of Recent Books

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End-to-end repair of aortic coarctation using absorbable polydioxanone suture (Arenas, Myers, & others) 1991;51: 413–7*
Optimal age for repair of aortic coarctation (van Son, Daniëls, & Lacquet) 1991;51:344–5,CP
Risk of reintervention after coarctation repair (van Son & Lacquet) 1991;51:521,CP; Reply (Kron) 1991;51:522,CP
Aortic disease
Aortic atresia with normal left ventricle (Serraf, Bruniax, & others) 1991;51:1017–9,CR
Aortic valve
Replacement of the aortic valve or root with a pulmonary autograft in children (Gerosa, McKay, & Ross) 1991;91: 424–9*
Aortic valve insufficiency
Aortic regurgitation after left ventricular myotomy and myectomy (Brown, Roberts, & others) 1991;51:585–92*
Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair (Shapira, Fernandez, & others) 1991;51:969–72*
Management of aortic insufficiency in chronic aortic dissection (Pêgo-Fernandes, Stolf, & others) 1991;51:438–42*
Traumatic aortic insufficiency (Bex, Grande, & Deveze) 1991; 51:694–5,CP
Aortic valve stenosis
Supravalvar aortic stenosis: a 29-year review of surgical experience (Sharma, Fujiwara, & others) 1991,51:1031–9,CV
Supravalvar aortic stenosis (Doty) 1991;51:886–7,ED
Aortocoronary bypass. *See* Coronary artery bypass
Aprotinin
Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass (Harder, Eijsman, & others) 1991;51:936–41*
Arrhythmias
Amiodarone versus bretylium for suppression of reperfusion arrhythmias in dogs (Rosalion, Snow, & others) 1991;51: 81–5*
Heterotopic heart transplantation and native heart ventricular arrhythmias (Kotliar, Smart, & others) 1991;51:987–91*
Prevention of arrhythmias after noncardiac thoracic operations: flecainide versus digoxin (Borgeat, Petropoulos, & others) 1991;51:964–8*
Arterial switch operation
Arterial switch procedure in an adult (Trehan & Ott) 1991;51: 122–4,CR
False aneurysm formation of the great arteries after arterial switch operation (Kato, Nakada, & others) 1991;51:495–6,CR
Hemolysis due to branch pulmonary stenosis after the arterial switch procedure (Schroeder, Albert, & others) 1991;51: 491–2,CR
Long-term results after atrial correction of complete transposition of the great arteries (Merlo, De Tommasi, & others) 1991;51:227–31*

Arteries
- Acute vascular trauma (Tutassaura) 1991;51:1044–5,CP
- Technique for use of the inferior epigastric artery as a coronary bypass graft (Mills & Everson) 1991;51:208–14*

Ascites
- Ascites after rupture of dissecting aortic aneurysm into the right atrium (Henze, Thorelius, & others) 1991;51:125–7,CR

Asphyxia
- Traumatic asphyxia (Lee, Wong, & others) 1991;51:86–8*

Aspirin
- Aspirin and blood loss (Violaris & Angelini) 1991;51:693,CP; Reply (Taggart, Siddiqui, & Wheatley) 1991;51:693–4,CP

Assisted circulation
- Comparison of hemodynamics and ejection fraction during left heart bypass (Sekela, Verani, & Noon) 1991;51:804–6*
- Mechanical circulatory assistance after heart transplantation (Emery, Eales, & others) 1991;51:43–4*
- Postcardiotomy mechanical circulatory support in the elderly (Wareing & Kouchoukos) 1991;51:441–7*

Atelectasis
- Altered cellular immune function in the atelectatic lung (Nguyen, Mulder, & Shennib) 1991;51:76–80*

Atrioventricular canal
- Atrioventricular canal defects (Capouya & Laks) 1991;51:860–3,KR

Autoantibodies
- Agglutination of blood cardioplegia by cold-reacting autoantibodies (Holman, Smith, & others) 1991;51:833–6,CR

Azathioprine
- Hemodynamics versus biopsy findings during cardiac transplant rejection (Bolling, Putnam, & others) 1991;51:52–5*
- The safety of low-dose prednisone before and immediately after heart-lung transplantation (Novick, Menkis, & others) 1991;51:642–5*

Balloon dilation
- Hemodynamic effects of lobar pulmonary artery occlusion in a porcine sepsis model (Ward, Shennib, & Zidulka) 1991;51:451–4*
- Membranotomy for Budd-Chiari syndrome (Cheng) 1991;51:522–3,CP; Reply (Victor, Jayanthi, & Madanagopalan) 1991;51:523,CP

Barnard, Christiaan
- Christiaan Barnard's contribution to the surgical treatment of Ebstein's malformation (Kirklin) 1991;51:147–51,CL

Barrett esophagus
- New surgical approach to complicated gastroesophageal reflux disease: transthoracic parietal cell vagotomy (Landreneau, Marshall, & others) 1991;51:128–30,CR

Behçet's disease
- Left ventricular aneurysm secondary to Behçet's disease (Di Eusanio, Mazzola, & others) 1991;51:131–2,CR

Bioprosthesis
- Atrioventricular valve replacement with a Hancock porcine xenograft (Cohn) 1991;51:683–5,CL

Biopsy
- Hemodynamics versus biopsy findings during cardiac transplant rejection (Bolling, Putnam, & others) 1991;51:52–5*

Biopsy, needle
- Role of percutaneous fine-needle aspiration biopsy in suspected intrathoracic malignancy (Colquhoun, Rosenthal, & Morton) 1991;51:390–3*

Björk-Shiley valve
- Intraoperative echocardiography of a dislodged Björk-Shiley mitral valve disc (Tanaka, Abe, & others) 1991;51:315–6,CR

Blood
- Benefit from combining blood conservation measures in cardiac operations (Jones, Rawitscher, & others) 1991;51;541–6*
- A new era in blood conservation (Goodnough & Geha) 1991;51;703–4,ED
- Six different hemofiltration devices for blood conservation in cardiac surgery (Boldt, Zickmann, & others) 1991;51:747–53*

Blood flow
- Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease (Johnsson, Algotsson, & others) 1991;51:579–84*
- Coronary pathology predicts conduction disturbances after coronary artery bypass grafting (Mosseri, Meir, & others) 1991;51:248–52*

Book reviews
- *AIDS and Surgery*, edited by Sim & Jefferies (Page) 1991;51:836,RV
- *Anesthesia for Cardiac Surgery* by DiNardo & Schwartz (Finch) 1991;51:763,RV
- *Aortic Valve, The*, by Thubrikar (Bolling) 1991;51:998,RV
- *Current Practice of Surgical Stapling*, edited by Ravitch, Steichen, & Welter (Gaskill) 1991;51:824,RV
- *Diagnosis of Diseases of the Chest*, by Fraser, Pare, Pare, Fraser, and Genereux (Levine) 1991;51:1016,RV
- *Heart and Brain, Brain and Heart*, edited by Refsum, Sulg, & Rasmussen (Lytle) 1991;51:666,RV
- *Heart and Heart-Lung Transplantation*, by Baumgartner, Reitz, & Achuff (Kriett) 1991;51:572,RV
- *Lung Cancer Chronicles*, by Meyer (Roe) 1991;51:654,RV
- *Pleural Diseases, Second Edition*, by Light (Fosburg) 1991;51:663,RV
- *Surgery for Heart Valve Disease*, edited by Bodnar (Coffin) 1991;51:799,RV
- *Thoracic Surgery*, edited by Pichelmaier, Schildberg (Guyton) 1991;51:955,RV
- *Wanderjahr: The Education of a Surgeon, Edward D. Churchill*, edited by Scannell (Ferguson) 1991;51:968,RV

Brain
- Brain protection during circulatory arrest (Crittenden, Roberts, & others) 1991:51;942–7*
- Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease (Johnsson, Algotsson, & others) 1991;51:579–84*

Bretylium compounds
- Amiodarone versus bretylium for suppression of reperfusion arrhythmias in dogs (Rosalion, Snow, & others) 1991;51:81–5*

Bronchi
- Are sutures better than staples for closing bronchi and pulmonary vessels? (Graeber, Collins, & others) 1991;51:901–5*

Bronchial fistula
- Empyema and bronchopleural fistula (Pairolero, Trastek, & Allen) 1991;51:157–8,KR

Bronchoalveolar carcinoma
- Bronchoalveolar carcinoma: factors affecting survival (Daly, Trastek, & others) 1991;51:368–77*

Bronchoalveolar lavage
- Bronchoalveolar lavage in lung transplantation (Shennib & Nguyen) 1991;51:335–40,CV

Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection (Shennib, Nguyen, & others) 1991;51:630–5*
Budd-Chiari syndrome
Membranotomy for Budd-Chiari syndrome (Cheng) 1991;51:522–3,CP; Reply (Victor, Jayanthi, & Madanagopalan) 1991;51:523,CP
Bypass
Comparison of hemodynamics and ejection fraction during left heart bypass (Sekela, Verani, & Noon) 1991;51:804–6*

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Calcium in neonatal cardioplegia (Robinson) 1991;51:1043–4,CP; Reply (Bove & Gallagher) 1991;51;1044,CP
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Calcium chloride
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Cannula
Apical aortic cannulation: application of an old method with new paraphernalia (Robicsek) 1991;51:330–2,HW
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Carcinoembryonic antigen
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Carcinoma, bronchogenic
Bronchogenic carcinoma with chest wall invasion (Allen, Mathisen, & others) 1991;51:948–51*
Multiple primary bronchogenic carcinomas: treatment and follow-up (Fleisher, McElvaney, & Robinson) 1991;51:48–51*
Carcinoma, non-small cell lung
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Carcinoma, squamous cell
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Squamous cell carcinoma arising in a sternotomy scar (Korula & Hughes) 1991;51:667–9,CR
Carcinosarcoma
Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy (Meade, Moad, & others) 1991;51:488–90,CR
Cardiac output, low
Pulmonary artery balloon counterpulsation for intraoperative right ventricular failure (Skillington, Couper, & others) 1991;51:658–60,CR
Pulmonary sequelae of prolonged total venoarterial bypass: evaluation with a new experimental model (Koul, Willen, & others) 1991;51:794–9*
Cardiac pacing, artificial
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Cardiac tamponade
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Calcium in neonatal cardioplegia (Robinson) 1991;51:1043–4,CP; Reply (Bove & Gallagher) 1991;51;1044,CP
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Continuous warm blood cardioplegia (Tutassaura) 1991;51:866,CP
Efficacy of coronary sinus cardioplegia in patients with complete coronary artery occlusion (Menasché, Subayi, & others) 1991;51:418–23*
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Optimizing myocardial hypothermia: II. Cooling jacket modifications and clinical results (Daily & Kinney) 1991;51:284–9*
Oxygenated cardioplegia: the metabolic and functional effects of glucose and insulin (Steinberg, Doherty, & others) 1991;51:620–9*
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Cardiopulmonary bypass
Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass (Harder, Eijsman, & others) 1991;51:936–41*
Benefit from combining blood conservation measures in cardiac operations (Jones, Rawitscher, & others) 1991;51;541–6*

Cardiopulmonary bypass (cont'd)

- Cavoatrial tumor thrombectomy using cardiopulmonary bypass without circulatory arrest (Stewart, Carey, & others) 1991;51:717–22*
- Complement activation and lung permeability during cardiopulmonary bypass (Davies, Bailey, & others) 1991;51:695–6,CP; Reply (Tennenberg) 1991;51:696,CP
- Intraoperative management of severe endobronchial hemorrhage (Purut, Scott, & others) 1991;51:304–7,CR
- Membrane oxygenator prevents lung reperfusion injury in canine cardiopulmonary bypass (Gu, Wang, & others) 1991;51:573–8*
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- Prospects for understanding and eliminating the deleterious effects of cardiopulmonary bypass (Kirklin) 1991;51:529–31,ED
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- Technique and pitfalls of retrograde continuous warm blood cardioplegia (Salerno, Christakis, & others) 1991;51:1023–5,HW

Carotid artery disease

- Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease (Johnsson, Algotsson, & others) 1991;51:579–84*
- Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid disease (Allen) 1991;51:532–3,ED

Case reports

- Adenocarcinoma arising in a foregut cyst of the mediastinum (Olsen, Clemmensen, & Andersen) 1991;51:497–9,CR
- Agglutination of blood cardioplegia by cold-reacting autoantibodies (Holman, Smith, & others) 1991;51:833–6,CR
- Aortic atresia with normal left ventricle (Serraf, Bruniax, & others) 1991;51:1017–9,CR
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- Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy (Meade, Moad, & others) 1991;51:488–90,CR
- Delayed death from aortic root trauma (Boruchow & Hutchins) 1991;51:315–9,CR
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- Orthotopic cardiac transplantation in two patients with previous malignancy (Hinkamp, Sullivan, & others) 1991;51:1004–6,CR
- Palliative repair of aortic atresia associated with tricuspid atresia and transposition of the great arteries (Imai, Kurosawa, & others) 1991;51:646–8,CR
- Penetrating trauma involving the innominate artery (McLean & McManus) 1991;51:113–5, CR
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- Pericardial cyst with partial erosion of the right ventricular wall (Chopra, Duke, & others) 1991;51:840–1,CR
- Pneumonectomy secondary to *Mycobacterium fortuitum* in infancy (Paone, Mercer, & Glass) 1991;51:1010–1,CR
- Preoperative erythropoietin in Jehovah's Witnesses who require cardiac procedures (Gaudiani & Mason) 1991;51:823–4,CR
- Primary cardiac leiomyosarcomas (Antunes, Vanderdonck, & others) 1991;51:999–1001,CR
- Procainamide-induced respiratory insufficiency after cardiopulmonary bypass (Putnam, Bolling, & Kirsh) 1991;51:482–3,CR

Pulmonary artery balloon counterpulsation for intraoperative right ventricular failure (Skillington, Couper, & others) 1991;51:658–60,CR
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Sinus of Valsalva aneurysm eroding into the interventricular septum (Raffa, Mosieri, & others) 1991;51:996–8,CR
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Squamous cell carcinoma arising in a sternotomy scar (Korula & Hughes) 1991;51:667–9,CR
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Percutaneous transaortic closure of postinfarctional ventricular septal rupture (Hachida, Nakano, & others) 1991;51:655–7,CR
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Unifocalization for pulmonary atresia with ventricular septal defect (Puga) 1991;51:8–9,ED
Heart septum
The Senning operation: a new technique to prepare the septal flap (Assad, Felipe, & others) 1991;51:678–9,HW
Sinus of Valsalva aneurysm eroding into the interventricular septum (Raffa, Mosieri, & others) 1991;51:996–8,CR
Heart surgery
Aortic atresia with normal left ventricle (Serraf, Bruniax, & others) 1991;51:1017–9,CR
Aortic regurgitation after left ventricular myotomy and myectomy (Brown, Roberts, & others) 1991;51:585–92*
Autogenous atrial tunnel for direct cavopulmonary connection in infants and small children (Perryman) 1991;51:508–10,HW
Autologous blood transfusion with recombinant human erythropoietin in heart operations (Watanabe, Fuse, & others) 1991;51:767–72*
Benefit from combining blood conservation measures in cardiac operations (Jones, Rawitscher, & others) 1991;51;541–6*
Cardiorespiratory responses to hypertonic saline solution in cardiac operations (Boldt, Zickmann, & others) 1991;51:610–5*
Combined superior-transseptal approach to the left atrium (Berreklouw, Ercan, & Schönberger) 1991;51:293–5*
Comparison of hemodynamics and ejection fraction during left heart bypass (Sekela, Verani, & Noon) 1991;51:804–6*
Current surgical technique to repair Fallot's tetralogy with absent pulmonary valve syndrome (Snir, de Leval, & others) 1991;51:979–82*
Delayed sternal closure for life-threatening complications in cardiac operations: an update (Mestres, Pomar, & others) 1991;51:773–6*
Diagnosis of poststernotomy infection: comparison of three means of assessment (Browdie, Bernstein, & others) 1991;51:290–2*
Dopamine and high-dose insulin infusion (glucose-insulin-potassium) after a cardiac operation: effects on myocardial metabolism (Svedjeholm, Hallhagen, & others) 1991;51:262–70*
Dynamic cardiomyoplasty in chronic Chagas' heart disease: clinicopathological data (Rossi, Braile, & others) 1991;51:649–51,CR
The Fontan procedure: a historical review (Cowgill) 1991;51:1026–30,CL
Hemi-Fontan operation in surgery for single ventricle: a preliminary report (Douville, Sade, & Fyfe) 1991;51:893–900*
Hemolysis after valve repair (Bloom, Goldman, & others) 1991;51:526,CP
Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair (Shapira, Fernandez, & others) 1991;51:969–72*
Long-term results after atrial correction of complete transposition of the great arteries (Merlo, De Tommasi, & others) 1991;51:227–31*
Palliation of univentricular heart without increasing work (Lamberti) 1991;51:882–3,ED
Patch aortotomy for aortic valve replacement after previous coronary artery bypass grafting (Sindhi, Belisle, & others) 1991;51:676–7,HW
Percutaneous transaortic closure of postinfarctional ventricular septal rupture (Hachida, Nakano, & others) 1991;51:655–7,CR
Postcardiotomy mechanical circulatory support in the elderly (Wareing & Kouchoukos) 1991;51:441–7*
Preoperative erythropoietin in Jehovah's Witnesses who require cardiac procedures (Gaudiani & Mason) 1991;51:823–4,CR
Pulmonary sequelae of prolonged total venoarterial bypass: evaulation with a new experimental model (Koul, Willen, & others) 1991;51:794–9*
Reoperation for persistent outflow obstruction in hypertrophic cardiomyopathy (Roberts, McIntosh, & others) 1991;51:453–60*
Risk factors for cardiac operations in adult Jehovah's Witnesses (Lewis, Murphy, & Cooley) 1991;51:448–50*
Risk of reintervention after coarctation repair (van Son & Lacquet) 1991;51:521,CP; Reply (Kron) 1991;51:522,CP
The Senning operation: a new technique to prepare the septal flap (Assad, Felipe, & others) 1991;51:678–9,HW
Single drain (pleura, pericardium, mediastinum) after open heart operations (Victor & Kabeer) 1991;51:345–6,CP; Reply (Moulijn, Smulders, & others) 1991;51:346,CP
Single venous cannulation through the right atrium for venous return in valve operations (Balasundaram, Vega, & Duran) 1991;51:506–7,HW
Six different hemofiltration devices for blood conservation in cardiac surgery (Boldt, Zickmann, & others) 1991;51:747–53*
Supravalvar aortic stenosis: a 29–year review of surgical experience (Sharma, Fujiwara, & others) 1991,51:1031–9,CV
Supravalvar aortic stenosis (Doty); 1991;51:886–7,ED
Surgical management of carcinoid heart disease (Fetherston & Davis) 1991;51:493–4,CR
Temporary external DDD pacing after cardiac operations (Ferguson & Cox) 1991;51:723–32*
Tricuspid valve repair for tricuspic valve endocarditis: tricuspid valve "recycling" (Allen, Slachman, & others) 1991;51:593–8*
Uncomfortable issues (Bilfinger) 1991;51:347,CP; Reply (Edmunds) 1991;51:347–8,CP
When do cerebral emboli appear during open heart operations? A transcranial Doppler study (van der Linden & Casimir-Ahn) 1991;51:237–41*
Heart transplantation
Hemodynamics versus biopsy findings during cardiac transplant rejection (Bolling, Putnam, & others) 1991;51:52–5*
Heterotopic heart transplantation and native heart ventricular arrhythmias (Kotliar, Smart, & others) 1991;51:987–91*
Mechanical circulatory assistance after heart transplantation (Emery, Eales, & others) 1991;51:43–7*
Mitral valve replacement six years after cardiac transplantation (Copeland, Rosado, & others) 1991;51:1014–6,CR

Heart transplantation (cont'd)

- Orthotopic cardiac transplantation in two patients with previous malignancy (Hinkamp, Sullivan, & others) 1991;51: 1004–6,CR
- An unusual complication of cardiac transplantation—infected aortic pseudoaneurysm (Palac, Strausbaugh, & others) 1991;55:479–81,CR

Heart valve prosthesis

- Atrioventricular valve replacement with a Hancock porcine xenograft (Cohn) 1991;51:683–5,CL
- Binding of preformed xenoantibodies to porcine bioprosthetic valves (Sanchez, Marboe, & others) 1991;51:30–3*
- Christiaan Barnard's contribution to the surgical treatment of Ebstein's malformation (Kirklin) 1991;51:147–51,CL
- Comparison of supraannular and subannular pledgeted sutures in mitral valve replacement (Chambers & Heath) 1991;51:60–3*
- Endothelial cell viability in the rat aortic wall (Christy, Lupinetti, & others) 1991;51:204–7*
- Failure of Hancock pericardial xenografts: is prophylactic bioprosthetic replacement justified? (Bortolotti, Milano, & others) 1991;51:430–7*
- The first mitral valve replacement (Norman) 1991;51:525–6,CP
- Intraoperative echocardiography of a dislodged Björk-Shiley mitral valve disc (Tanaka, Abe, & others) 1991;51:315–6,CR
- Long-term results of Ionescu-Shiley valve in the tricuspid position (Eng, Ravichandran, & others) 1991;51:200–3*
- Management of aortic insufficiency in chronic aortic dissection (Pêgo-Fernandes, Stolf, & others) 1991;51:438–42*
- Mitral valve replacement combined with coronary artery operation: determinants of early and late results (He, Hughes, & others) 1991;51:916–23*
- Mitral valve replacement in idiopathic hypereosinophilic syndrome (Boustany, Murphy, & others) 1991;51 1007–9,CR
- Mitral valve replacement six years after cardiac transplantation (Copeland, Rosado, & others) 1991;51:1014–6,CR
- Patch aortotomy for aortic valve replacement after previous coronary artery bypass grafting (Sindhi, Belisle, & others) 1991;51:676–7,HW
- Reoperation for persistent outflow obstruction in hypertrophic cardiomyopathy (Roberts, McIntosh, & others) 1991;51: 453–60*
- The Starr valve revisited (Pluth) 1991;51:333–4,CL
- Traumatic mitral valve rupture in a child (McCrory, Craig, & O'Kane) 1991;51:821–2,CR
- Valve replacement in patients with endocarditis and cerebral septal emboli (Ting, Silverman, & Levitsky) 1991;51:18–22*
- Valve re-replacement in the asymptomatic patient (Cohn) 1991;51:357–8,ED
- When do cerebral emboli appear during open heart operations? A transcranial Doppler study (van der Linden & Casimir-Ahn) 1991;51:237–41*

Heart ventricle

- Aortic atresia with normal left ventricle: one-stage repair in early infancy (Bogers, Sreeram, & others) 1991;51:312–4*
- Aortic regurgitation after left ventricular myotomy and myectomy (Brown, Roberts, & others) 1991;51:585–92*
- Effects of calcium chloride administration on the postischemic isolated rat heart (Abbott, Hill, & others) 1991;51:705–10*
- Fibrous skeleton and ventricular outflow tracts in double-outlet right ventricle (Howell, Ho, & others) 1991;51:394–400*
- The Fontan procedure: a historical review (Cowgill) 1991;51: 1026–30,CL
- Hemi-Fontan operation in surgery for single ventricle: a preliminary report (Douville, Sade, & Fyfe) 1991;51:893–900*
- Left ventricular pseudoaneurysm with hemoptysis (Adkins, Laub, & others) 1991;51:476–8,CR
- Palliation of univentricular heart without increasing work (Lamberti) 1991;51:882–3,ED
- Pericardial cyst with partial erosion of the right ventricular wall (Chopra, Duke, & others) 1991;51:840–1,CR
- Pretreatment with nicardipine preserves ventricular function after hypothermic ischemic arrest (Brown, Parenteau, & others) 1991;51:739–46*
- Repair of posterior left ventricular aneurysm in a six-year-old boy (Grossi, Colvin, & others) 1991;51:484–7,CR
- Ventricular perforation with valvoplasty (Smith) 1991;51:1042–3,CP; Reply (Robertson) 1991;51:1043,CP

Hematocrit

- Erythropoietin deficiency after coronary artery bypass procedures (Levine, Rosen, & others) 1991;51:764–6*

Hemodynamics

- Comparison of hemodynamics and ejection fraction during left heart bypass (Sekela, Verani, & Noon) 1991;51:804–6*
- Hemodynamics versus biopsy findings during cardiac transplant rejection (Bolling, Putnam, & others) 1991;51:52–5*
- Heterotopic heart transplantation and native heart ventricular arrhythmias (Kotliar, Smart, & others) 1991;51:987–91*
- Pulmonary sequelae of prolonged total venoarterial bypass: evaulation with a new experimental model (Koul, Willen, & others) 1991;51:794–9*
- Staged repair of pulmonary atresia with ventricular septal defect and major systemic to pulmonary artery collaterals (Iyer & Mee) 1991;51:65–72*

Hemofiltration

- Six different hemofiltration devices for blood conservation in cardiac surgery (Boldt, Zickmann, & others) 1991;51:747–53*

Hemolysis

- Hemolysis after valve repair (Bloom, Goldman, & others) 1991;51:526,CP
- Hemolysis due to branch pulmonary stenosis after the arterial switch procedure (Schroeder, Albert, & others) 1991;51: 491–2,CR

Hemoptysis

- Left ventricular pseudoaneurysm with hemoptysis (Adkins, Laub, & others) 1991;51:476–8,CR

Hemorrhage

- Aspirin and blood loss (Violaris & Angelini) 1991;51:693,CP; Reply (Taggart, Siddiqui, & Wheatley) 1991;51:693–4,CP
- False aneurysm formation of the great arteries after arterial switch operation (Kato, Nakada, & others) 1991;51:495–6,CR
- Intraoperative management of severe endobronchial hemorrhage (Purut, Scott, & others) 1991;51:304–7,CR
- Management of endobronchial hemorrhage (Feng & Singh) 1991;51:1045–6,CP
- Use of human recombinant erythropoietin to correct severe preoperative anemia (Fullerton, Campbell, & Whitman) 1991;51:825–6,CR

Hemostasis

- Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass (Harder, Eijsman, & others) 1991;51:936–41*

Heparin

- Potential use of recombinant hirudin as an anticoagulant in a cardiopulmonary bypass model (Walenga, Bakhos, & others) 1991;51:271–7*

Hepatic vein thrombosis
- Membranotomy for Budd-Chiari syndrome (Cheng) 1991;51:522–3,CP; Reply (Victor, Jayanthi, & Madanagopalan) 1991;51:523,CP

Hernia, hiatal
- Intrathoracic Nissen fundoplication: long-term clinical and pH monitoring evaluation (Collard, Konick, & others) 1991;51:34–8*

Hirudin
- Potential use of recombinant hirudin as an anticoagulant in a cardiopulmonary bypass model (Walenga, Bakhos, & others) 1991;51:271–7*

Histiocytoma
- Malignant fibrous histiocytoma of the trachea (Streitz & Shapshay) 1991;51:695,CP; Reply (Mansour) 1991;51:695,CP

HIV
- Human immunodeficiency virus and the thoracic surgeon (Stiles) 1991;51:341–3,RE

Hodgkin's disease
- Total unilateral lung gangrene in Hodgkin's disease: treatment by thoracostomy (Juettner, Arian-Schad, & others) 1991;51:302–3,CR

How to do it
- Alternative technique for repair of sinus venosus atrial septal defect (Hamilton, Brooks, & Walker) 1991;51:144–6,HW
- Apical aortic cannulation: application of an old method with new paraphernalia (Robicsek) 1991;51:330–2,HW
- Autogenous atrial tunnel for direct cavopulmonary connection in infants and small children (Perryman) 1991;51:508–10,HW
- Continuous retrograde blood cardioplegia (Sutter, Goldman, & others) 1991;51:136–7,HW
- Coronary ostial reconstruction: technical issues (Ghosh) 1991;51:673–5,HW
- Dissectors for pulmonary thromboendarterectomy (Daily, Dembitsky, & Daily) 1991;51:842–3,HW
- Easy removal of surgically placed intraaortic balloon pump catheter (Gorton & Soltanzadeh) 1991;51:325–6,HW
- Exchanging double-lumen for single-lumen endotracheal tubes after thoracotomy (Rusch, Freund, & Bowdle) 1991;51:321–4,HW
- Improved technique for inserting a T tube in patients with subglottic stenosis (Kato, Kobayashi, & others) 1991;51;327–9,HW
- Intraoperative coronary angiography using fluorescein (Takayama, Wanibuchi, & others) 1991;51:140–3,HW
- Mammary artery grafts: a new no-touch technique for anastomosis (Galvin) 1991;51:500–3,HW
- New operative method for distal aortopulmonary septal defect (Kitagawa, Katoh, & others) 1991;51:680–2,HW
- New technique of esophageal exclusion for chronic esophageal perforation (Lee, Lee, & Chu) 1991;51:1020–2,HW
- Patch aortotomy for aortic valve replacement after previous coronary artery bypass grafting (Sindhi, Belisle, & others) 1991;51:676–7,HW
- Pleural anesthetics given through an epidural catheter secured inside a chest tube (Baker & Tribble) 1991;51:138–9,HW
- Reinforced sternal closure (Scovotti, Ponzone, & Leyro-Diaz) 1991;51:844–5,HW
- The Senning operation: a new technique to prepare the septal flap (Assad, Felipe, & others) 1991;51:678–9,HW
- Silicone pouch for protection of automatic implantable cardioverter-defibrillator leads (Cilley, Cernaianu, & others) 1991;51:504–5,HW
- Simplified method for femoral venous cannulation (Rosenbloom & Musket) 1991;51:846–7,HW
- Single venous cannulation through the right atrium for venous return in valve operations (Balasundaram, Vega, & Duran) 1991;51:506–7,HW
- Technique and pitfalls of retrograde continuous warm blood cardioplegia (Salerno, Christakis, & others) 1991;51:1023–5,HW

Hydrogen-ion concentration
- Intrathoracic Nissen fundoplication: long-term clinical and pH monitoring evaluation (Collard, Konick, & others) 1991;51:34–8*
- Metabolism of the heart and brain during hypothermic cardiopulmonary bypass (Swain, McDonald & others) 1991;51:103–9*

Hypercalcemia
- Effects of calcium chloride administration on the postischemic isolated rat heart (Abbott, Hill, & others) 1991;51:705–10*

Hypertension, pulmonary
- Hemodynamic effects of lobar pulmonary artery occlusion in a porcine sepsis model (Ward, Shennib, & Zidulka) 1991;51:451–4*
- Pulmonary hypertension and polymorphonuclear leukocyte elastase after esophageal cancer operations (Sato, Murakami, & others) 1991;51:754–8*

Hypertrophy
- Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy (Meade, Moad, & others) 1991;51:488–90,CR
- Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair (Shapira, Fernandez, & others) 1991;51:969–72*

Hypopharynx
- Gastric emptying after gastric interposition for cancer of the esophagus or hypopharynx (Morton, Karwande, & others) 1991;51:759–63*

Hypoplasia
- Aortic atresia with normal left ventricle: one-stage repair in early infancy (Bogers, Sreeram, & others) 1991;51:312–4*

Hypothermia
- Brain protection during circulatory arrest (Crittenden, Roberts, & others) 1991:51;942–7*
- Metabolism of the heart and brain during hypothermic cardiopulmonary bypass (Swain, McDonald & others) 1991;51:103–9*
- Optimizing myocardial hypothermia: I. Temperature probe design and clinical inferences (Kinney, Daily, & Pfeffer) 1991;51:278–83*
- Optimizing myocardial hypothermia: II. Cooling jacket modifications and clinical results (Daily & Kinney) 1991;51:284–9*

Immunity, cellular
- Altered cellular immune function in the atelectatic lung (Nguyen, Mulder, & Shennib) 1991;51:76–80*

Infant
- Aortic atresia with normal left ventricle: one-stage repair in early infancy (Bogers, Sreeram, & others) 1991;51:312–4*
- Aortic atresia with normal left ventricle (Serraf, Bruniax, & others) 1991;51:1017–9,CR
- Autogenous atrial tunnel for direct cavopulmonary connection in infants and small children (Perryman) 1991;51:508–10,HW
- Calcium in neonatal cardioplegia (Robinson) 1991;51:1043–4,CP; Reply (Bove & Gallagher) 1991;51;1044,CP

Infant (cont'd)

Early restenosis after extended end-to-end anastomosis at neonatal age (van Son, Smedts, & Lacquet) 1991;51:160–2,CP; Reply (Elliott) 1991;51:162,CP

False aneurysm formation of the great arteries after arterial switch operation (Kato, Nakada, & others) 1991;51:495–6,CR

Hemolysis due to branch pulmonary stenosis after the arterial switch procedure (Schroeder, Albert, & others) 1991;51:491–2,CR

New operative method for distal aortopulmonary septal defect (Kitagawa, Katoh, & others) 1991;51:680–2,HW

Palliation of univentricular heart without increasing work (Lamberti) 1991;51:882–3,ED

Pneumonectomy secondary to *Mycobacterium fortuitum* in infancy (Paone, Mercer, & Glass) 1991;51:1010–1 CR

Progress of patients with pulmonary atresia after systemic to pulmonary arterial shunts (Calder, Chan, & others) 1991;51:401–7*

Risk of reintervention after coarctation repair (van Son & Lacquet) 1991;51:521,CP; Reply (Kron) 1991;51:522,CP

Infection

Diagnosis of poststernotomy infection: comparison of three means of assessment (Browdie, Bernstein, & others) 1991;51:290–2*

Infected intravenous port device causing tricuspid valve regurgitation (Heinemann, Frank, & others) 1991;51:827–8,CR

Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection (Shennib, Nguyen, & others) 1991;51:630–5*

Randomized trial of one-dose versus six-dose cefazolin prophylaxis in elective general thoracic surgery (Olak, Jeyasingham, & others) 1991;51:956–8*

Innominate artery

Penetrating trauma involving the innominate artery (McLean & McManus) 1991;51:113–5,CR

Insulin

Could glucose-insulin-potassium be considered only a step of a complete nutritional program for complicated cardiac patients? (Paccagnella, Simini, & Valfré) 1991;51:344,CP

Dopamine and high-dose insulin infusion (glucose-insulin-potassium) after a cardiac operation: effects on myocardial metabolism (Svedjeholm, Hallhagen, & others) 1991;51:262–70*

Oxygenated cardioplegia: the metabolic and functional effects of glucose and insulin (Steinberg, Doherty, & others) 1991;51:620–9*

Intraaortic balloon pumping

Easy removal of surgically placed intraaortic balloon pump catheter (Gorton & Soltanzadeh) 1991;51:325–6,HW

Irrigation

Bronchoalveolar lavage in lung transplantation (Shennib & Nguyen) 1991;51:335–40,CV

Intraoperative pleural lavage cytology in lung cancer patients (Okumura, Ohshima, & others) 1991;51:599–604*

Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection (Shennib, Nguyen, & others) 1991;51:630–5*

Thoracoscopic debridement and pleural irrigation in the management of empyema thoracis (Ridley & Braimbridge) 1991;51:461–4*

Ischemia

Effects of calcium chloride administration on the postischemic isolated rat heart (Abbott, Hill, & others) 1991;51:705–10*

Pretreatment with nicardipine preserves ventricular function after hypothermic ischemic arrest (Brown, Parenteau, & others) 1991;51:739–46*

Reducing postischemic paraplegia using conjugated superoxide dismutase (Agee, Flanagan, & others) 1991;51:911–5*

Surgical repair of Wolff-Parkinson-White syndrome complicated with myocardial bridging (Sueda, Matsuura, & others) 1991;51:119–121,CR

Triiodothyronine in the recovery of stunned myocardium in dogs (Novitsky, Matthews, & others) 1991;51:10–17*.

Jehovah's Witnesses. *See* Heart surgery

Jejunoileal bypass

Late volume changes in retrosternal colon bypass (Santos) 1991;51:296–8,CR

Key references

Atrioventricular canal defects (Capouya & Laks) 1991;51:860–3,KR

Empyema and bronchopleural fistula (Pairolero, Trastek, & Allen) 1991;51:157–8,KR

Mediastinal masses (Silverman) 1991;51:520,KR

Killer cells, natural

Altered cellular immune function in the atelectatic lung (Nguyen, Mulder, & Shennib) 1991;51:76–80*

Laser

Excimer laser angioplasty during aortocoronary bypass grafting (Blanche, Segalowitz, & others) 1991;51:670–2,CR

Neodymium:yttrium-aluminum garnet laser-assisted pulmonary resections (Landreneau, Hazelrigg, & others) 1991;51:973–8*

Leiomyosarcoma

Primary cardiac leiomyosarcomas (Antunes, Vanderdonck, & others) 1991;51:999–1001,CR

Rectus abdominis muscle flap with microvascular anastomoses for repair of recurrent sarcoma (Waris, Kaarela, & others) 1991;51:133–5,CR

Lidocaine

Spinal cord protection during aortic occlusion: efficacy of intrathecal tetracaine (Breckwoldt, Genco, & others) 1991;51:959–63*

Liposarcoma

Liposarcoma of the esophagus (Cooper, Boucher, & others) 1991;51:1012–3,CR

Lung

Complement activation and lung permeability during cardiopulmonary bypass (Davies, Bailey, & others) 1991;51:695–6,CP; Reply (Tennenberg) 1991;51:696,CP

Membrane oxygenator prevents lung reperfusion injury in canine cardiopulmonary bypass (Gu, Wang, & others) 1991;51:573–8*

Lung disease

Pneumonectomy secondary to *Mycobacterium fortuitum* in infancy (Paone, Mercer, & Glass) 1991;51:1010–1,CR

Total unilateral lung gangrene in Hodgkin's disease: treatment by thoracostomy (Juettner, Arian-Schad, & others) 1991;51:302–3,CR

Lung neoplasms

Aggressive surgical intervention in N2 non–small cell cancer of the lung (Watanabe, Shimizu, & others) 1991;51:253–61*

Bronchoalveolar carcinoma: factors affecting survival (Daly, Trastek, & others) 1991;51:368–77*

- Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy (Meade, Moad, & others) 1991;51:488–90,CR
- Chest wall involvement by lung cancer: computed tomographic detection and results of operation (Ratto, Piacenza, & others) 1991;51:182–7*
- Computed tomography–guided minithoracotomy for the resection of small peripheral pulmonary nodules (Daly, Faling, & others) 1991;51:465–9*
- Intraoperative pleural lavage cytology in lung cancer patients (Okumura, Ohshima, & others) 1991;51:599–604*
- Multiple primary bronchogenic carcinomas: treatment and follow-up (Fleisher, McElvaney, & Robinson) 1991;51:48–51*
- Nephrotic syndrome complicating adenocarcinoma of the lung with resolution after resection (Coltharp, Lee, & others) 1991;51:308–9,CR
- Response to chemotherapy does not predict survival after resection of sarcomatous pulmonary metastases (Lanza, Putnam, & others) 1991;51:219–24*
- Staging lung cancer with computed tomography (Goldstraw) 1991;51:345,CP; Reply (Lewis) 1991;51:345,CP

Lung transplantation
- Bronchoalveolar lavage in lung transplantation (Shennib & Nguyen) 1991;51:335–40,CV
- Enhanced pulmonary function using dimethylthiourea for twelve-hour lung preservation (Lambert, Egan, & others) 1991;51:924–30*
- Improved lung preservation with cold air storage (Kon, Hines, & others) 1991;51:557–62*
- Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection (Shennib, Nguyen, & others) 1991; 51:630–5*

Lymphoma
- Primary cysts and tumors of the mediastinum (Cohen, Thompson, & others) 1991;51:378–86*

Magnesium
- Magnesium ion is beneficial in hypothermic crystalloid cardioplegia (Brown, Holland, & others) 1991;51:359–67*

Magnetic resonance imaging
- Metallic surgical clips and magnetic resonance imaging (Weber) 1991;51:162,CP; Reply (Gold) 1991;51:162–3,CP

Malignant carcinoid syndrome
- Surgical management of carcinoid heart disease (Fetherston & Davis) 1991;51:493–4,CR

Mammary artery
- Comparison of postoperative complications between saphenous vein and IMA grafts to left anterior descending coronary artery (Sethi, Copeland, & others) 1991;51:733–8*
- False aneurysm of the right internal mammary artery (Millner, Guvendik, & others) 1991;51:831–2,CR
- Inverted internal mammary artery for myocardial revascularization (Livi, Bortolotti, & Gallucci) 1991;51:524–5,CP
- Long-term follow-up of the Vineberg internal mammary artery implant procedure (Hayward, Korompai, & Knight) 1991; 51:1002–3,CR
- Mammary artery grafts: a new no-touch technique for anastomosis (Galvin) 1991;51:500–3,HW
- Pharmacological response of internal mammary artery and gastroepiploic artery (van Son & Smedts) 1991;51:864,CP; Reply (Koike & Suma) 1991;51:864–5,CP

Mediastinal cyst
- Adenocarcinoma arising in a foregut cyst of the mediastinum (Olsen, Clemmensen, & Andersen) 1991;51:497–9,CR
- Pericardial cyst with partial erosion of the right ventricular wall (Chopra, Duke, & others) 1991;51:840–1,CR
- Primary cysts and tumors of the mediastinum (Cohen, Thompson, & others) 1991;51:378–86*

Mediastinal neoplasms
- Mediastinal masses (Silverman) 1991;51:520,KR
- Primary cysts and tumors of the mediastinum (Cohen, Thompson, & others) 1991;51:378–86*
- Rupture of a benign mediastinal teratoma into the right pleural cavity (Hiraiwa, Hayashi, & others) 1991;51:110–12,CR

Mediastinitis
- Fibrosing mediastinitis with coronary artery involvement (Cochrane, Warren, & others) 1991;51:652–4,CR

Medical oncology
- Symposium on thoracic surgical oncology (Pass) 1991;51: 153,CP

Metabolism
- Metabolism of the heart and brain during hypothermic cardiopulmonary bypass (Swain, McDonald & others) 1991;51: 103–9*
- Oxygenated cardioplegia: the metabolic and functional effects of glucose and insulin (Steinberg, Doherty, & others) 1991;51:620–9*

Metals
- Metallic surgical clips and magnetic resonance imaging (Weber) 1991;51:162,CP; Reply (Gold) 1991;51:162–3,CP

Metastasis
- Bronchogenic carcinoma with chest wall invasion (Allen, Mathisen, & others) 1991;51:948–51*
- Response to chemotherapy does not predict survival after resection of sarcomatous pulmonary metastases (Lanza, Putnam, & others) 1991;51:219–24*

Mitochondria, heart
- Effects of calcium chloride administration on the postischemic isolated rat heart (Abbott, Hill, & others) 1991;51:705–10*

Mitral valve
- Combined superior-transseptal approach to the left atrium (Berreklouw, Ercan, & Schönberger) 1991;51:293–5*
- Hemolysis after valve repair (Bloom, Goldman, & others) 1991;51:526,CP
- Mitral prosthetic replacement in small left atria (Balasundaram & Duran) 1991;51:1046,CP; Reply (Campanella, Cameron, & Feilberg) 1991;51:1046–7,CP
- Mitral valve reoperation (Bonchek) 1991;51:160,CP
- Mitral valve replacement combined with coronary artery operation: determinants of early and late results (He, Hughes, & others) 1991;51:916–23*
- Mitral valve replacement in idiopathic hypereosinophilic syndrome (Boustany, Murphy, & others) 1991;51:1007–9,CR
- Mitral valve replacement six years after cardiac transplantation (Copeland, Rosado, & others) 1991;51:1014–6,CR
- Mitral valve suture techniques (Lemmer) 1991;51:865,CP; Reply (Heath) 1991;51:866,CP

Monitoring, physiologic
- Optimizing myocardial hypothermia: I. Temperature probe design and clinical inferences (Kinney, Daily, & Pfeffer) 1991;51:278–83*

Mortality
- Delayed death from aortic root trauma (Boruchow & Hutchins) 1991;51:315–9,CR
- Hospital mortality and long-term survival after pulmonary resection in the elderly (Roxburgh, Thompson, & Goldstraw) 1991;51:800–3*

Mortality (cont'd)
  Prospects for understanding and eliminating the deleterious effects of cardiopulmonary bypass (Kirklin) 1991;51:529–31,ED
  Risk factors for cardiac operations in adult Jehovah's Witnesses (Lewis, Murphy, & Cooley) 1991;51:448–50*
Myasthenia gravis
  Role of staging in prognosis and management of thymoma (Wilkins, Grillo, & others) 1991;51:888–92*
  Thymoma: results of 241 operated cases (Maggi, Casadio, & others) 1991;51:152–6,CV
Mycobacterium infections
  Pneumonectomy secondary to *Mycobacterium fortuitum* in infancy (Paone, Mercer, & Glass) 1991;51:1010–1,CR
Myocardial contraction
  Might free arterial grafts fail due to spasm? (Massa, Johansson, & others) 1991;51:94–101*
Myocardial infarction
  Delayed death from aortic root trauma (Boruchow & Hutchins) 1991;51:315–9,CR
  Nifedipine after coronary bypass grafting (Nathan) 1991;51:693,CP
  Percutaneous transaortic closure of postinfarctional ventricular septal rupture (Hachida, Nakano, & others) 1991;51:655–7,CR
Myocardial reperfusion
  Production of endothelium-derived contracting factor is enhanced after coronary reperfusion (Pearson & Lin) 1991;51:788–93*
Myocardial revascularization
  Combined myocardial revascularization and abdominal aortic aneurysm repair (Hinkamp, Pifarre, & others) 1991;51:470–2*
  Coronary ostial reconstruction: technical issues (Ghosh) 1991;51:673–5,HW
  Inverted internal mammary artery for myocardial revascularization (Livi, Bortolotti, & Gallucci) 1991;51:524–5,CP
  Long-term follow-up of the Vineberg internal mammary artery implant procedure (Hayward, Korompai, & Knight) 1991;51:1002–3,CR
Myocardium
  Dopamine and high-dose insulin infusion (glucose-insulin-potassium) after a cardiac operation: effects on myocardial metabolism (Svedjeholm, Hallhagen, & others) 1991;51:262–70*
  Optimizing myocardial hypothermia: I. Temperature probe design and clinical inferences (Kinney, Daily, & Pfeffer) 1991;51:278–83*
  Optimizing myocardial hypothermia: II. Cooling jacket modifications and clinical results (Daily & Kinney) 1991;51:284–9*
  Oxygenated cardioplegia: the metabolic and functional effects of glucose and insulin (Steinberg, Doherty, & others) 1991;51:620–9*
  Retrograde continuous warm blood cardioplegia: a new concept in myocardial protection (Salerno, Houck, & others) 1991;51:245–7*
  Superiority of retrograde cardioplegia after coronary occlusion (Haan, Lazar, & others) 1991;51:408–12*
  Surgical repair of Wolff-Parkinson-White syndrome complicated with myocardial bridging (Sueda, Matsuura, & others) 1991;51:119–21,CR
  Triiodothyronine in the recovery of stunned myocardium in dogs (Novitsky, Matthews, & others) 1991;51:10–17*

Neoplasms
  Adenocarcinoma arising in a foregut cyst of the mediastinum (Olsen, Clemmensen, & Andersen) 1991;51:497–9,CR
  Cavoatrial tumor thrombectomy using cardiopulmonary bypass without circulatory arrest (Stewart, Carey, & others) 1991;51:717–22*
  Cervical lymph node dissection for thoracic esophageal cancer (Skinner) 1991;51:884–5,ED
  Gastric emptying after gastric interposition for cancer of the esophagus or hypopharynx (Morton, Karwande, & others) 1991;51:759–63*
  Multiple primary bronchogenic carcinomas: treatment and follow-up (Fleisher, McElvaney, & Robinson) 1991;51:48–51*
  Orthotopic cardiac transplantation in two patients with previous malignancy (Hinkamp, Sullivan, & others) 1991;51:1004–6,CR
  Primary cysts and tumors of the mediastinum (Cohen, Thompson, & others) 1991;51:378–86*
  Role of percutaneous fine-needle aspiration biopsy in suspected intrathoracic malignancy (Colquhoun, Rosenthal, & Morton) 1991;51:390–3*
Nephrotic syndrome
  Nephrotic syndrome complicating adenocarcinoma of the lung with resolution after resection (Coltharp, Lee, & others) 1991;51:308–9,CR
Nerve block
  Site of action of continuous extracorporeal intercostal nerve block (Eng & Sabanathan) 1991;51:387–9*
Neutrophils
  Complement activation and lung permeability during cardiopulmonary bypass (Davies, Bailey, & others) 1991;51:695–6,CP; Reply (Tennenberg) 1991;51:696,CP
  Pulmonary hypertension and polymorphonuclear leukocyte elastase after esophageal cancer operations (Sato, Murakami, & others) 1991;51:754–8*
Nicardipine
  Pretreatment with nicardipine preserves ventricular function after hypothermic ischemic arrest (Brown, Parenteau & others) 1991;51:739–46*
Nifedipine
  Nifedipine after coronary bypass grafting (Nathan) 1991;51:693,CP
Nodules of Arantius
  Hypertrophy of nodules of Arantius and aortic insufficiency: pathophysiology and repair (Shapira, Fernandez, & others) 1991;51:969–72*
Norepinephrine
  Might free arterial grafts fail due to spasm? (Massa, Johansson, & others) 1991;51:94–101*
Nutrition
  Could glucose-insulin-potassium be considered only a step of a complete nutritional program for complicated cardiac patients? (Paccagnella, Simini, & Valfré) 1991;51:344,CP

Osteoarthropathy
  Carcinosarcoma of the lung with hypertrophic pulmonary osteoarthropathy (Meade, Moad, & others) 1991;51:488–90,CR
Oxygenation
  Oxygenation of cardioplegic solutions: a note of caution (Lochner, Lloyd, & Coetzee) 1991;51:777–87*
Oxygenator
  Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass (Harder, Eijsman, & others) 1991;51:936–41*

Membrane oxygenator prevents lung reperfusion injury in canine cardiopulmonary bypass (Gu, Wang, & others) 1991;51:573–8*
Prolonged pumpless arteriovenous perfusion for carbon dioxide extraction (Awad, Deslauriers, & others) 1991;51:534–40*
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Pacemaker, artificial
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Pain, postoperative
Pleural anesthetics given through an epidural catheter secured inside a chest tube (Baker & Tribble) 1991;51:138–9,HW
Palliative treatment
Palliative repair of aortic atresia associated with tricuspid atresia and transposition of the great arteries (Imai, Kurosawa, & others) 1991;51:646–8,CR
Prospective, randomized trial of palliative treatment for unresectable cancer of the esophagus (Reed, Marsh, & others) 1991;51:552–6*
Right pulmonary artery obstruction after pulmonary artery banding (Robertson, Penkoske, & Duncan) 1991;51:73–5*
Paraplegia
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Perfusion
Prolonged pumpless arteriovenous perfusion for carbon dioxide extraction (Awad, Deslauriers, & others) 1991;51:534–40*
Pericardium
Pericardial cyst with partial erosion of the right ventricular wall (Chopra, Duke, & others) 1991;51:840–1,CR
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Complement activation and lung permeability during cardiopulmonary bypass (Davies, Bailey, & others) 1991;51:695–6,CP; Reply (Tennenberg) 1991;51:696,CP
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Are sutures better than staples for closing bronchi and pulmonary vessels? (Graeber, Collins, & others) 1991;51:901–5*
Hemodynamic effects of lobar pulmonary artery occlusion in a porcine sepsis model (Ward, Shennib, & Zidulka) 1991;51:451–4*
Pleural effusion
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Pleural neoplasms
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Pneumonia
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Pneumonia, aspiration
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Postoperative complications
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Could glucose-insulin-potassium be considered only a step of a complete nutritional program for complicated cardiac patients? (Paccagnella, Simini, & Valfré) 1991;51:344,CP
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Role of potassium concentration in cardioplegic solutions in mediating endothelial damage (Mankad, Chester, & Yacoub) 1991;51:89–93*
Prednisone
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Procainamide-induced respiratory insufficiency after cardiopulmonary bypass (Putnam, Bolling, & Kirsh) 1991;51:482–3,CR
Prostaglandins
Prolonged preservation of canine lung allografts: the role of prostaglandins (Novick, Reid, & others) 1991;51:853–9,CV
Protective devices
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Enhanced pulmonary function using dimethylthiourea for twelve-hour lung preservation (Lambert, Egan, & others) 1991;51:924–30*

Pulmonary (cont'd)
Neodymium:yttrium-aluminum garnet laser-assisted pulmonary resections (Landreneau, Hazelrigg, & others) 1991;51:973–8*
Progress of patients with pulmonary atresia after systemic to pulmonary arterial shunts (Calder, Chan, & others) 1991;51:401–7*
Pulmonary sequelae of prolonged total venoarterial bypass: evaluation with a new experimental model (Koul, Willen, & others) 1991;51:794–9*
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Hemodynamic effects of lobar pulmonary artery occlusion in a porcine sepsis model (Ward, Shennib, & Zidulka) 1991;51:451–4*
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Unifocalization for pulmonary atresia with ventricular septal defect (Puga) 1991;51:8–9,ED
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Pulmonary embolism
Misplaced caval filter and subsequent pericardial tamponade (Lahey, Meyer, & others) 1991;51:299–301,CR
Pulmonary embolectomy (Beall) 1991;51:179,ED
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Pulmonary valve stenosis
Hemolysis due to branch pulmonary stenosis after the arterial switch procedure (Schroeder, Albert, & others) 1991;51:491–2,CR

Radiotherapy
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Gastrotracheal fistula as a result of radiotherapy after transhiatal esophagectomy (Paç, Başoğlu, & others) 1991;51:696–7,CP; Reply (Kron) 1991;51:697,CP
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Effects of calcium chloride administration on the postischemic isolated rat heart (Abbott, Hill, & others) 1991;51:705–10*
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Spinal cord protection during aortic occlusion: efficacy of intrathecal tetracaine (Breckwoldt, Genco, & others) 1991;51:959–63*
Report
Human immunodeficiency virus and the thoracic surgeon (Stiles) 1991;51:341–3,RE
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Rib fracture complicating median sternotomy (Gumbs, Peniston, & others) 1991;51:952–5*
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Hemi-Fontan operation in surgery for single ventricle: a preliminary report (Douville, Sade, & Fyfe) 1991;51:893–900*
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Traumatic mitral valve rupture in a child (McCrory, Craig, & O'Kane) 1991;51:821–2,CR

Saline solution, hypertonic
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Comparison of postoperative complications between saphenous vein and IMA grafts to left anterior descending coronary artery (Sethi, Copeland, & others) 1991;51:733–8*
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Sinus of Valsalva aneurysm eroding into the interventricular septum (Raffa, Mosieri, & others) 1991;51:996–8,CR
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Circulatory support 1991 1991;51:698–700, 1048–50
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Sutures
- Are sutures better than staples for closing bronchi and pulmonary vessels? (Graeber, Collins, & others) 1991;51:901–5*
- Comparison of supraannular and subannular pledgeted sutures in mitral valve replacement (Chambers & Heath) 1991;51:60–3*
- Delayed chest wall pain due to sternal wire sutures (Eastridge, Mahfood, & others) 1991;51:56–9*
- End-to-end repair of aortic coarctation using absorbable polydioxanone suture (Arenas, Myers, & others) 1991;51:413–7*
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- Rupture of a benign mediastinal teratoma into the right pleural cavity (Hiraiwa, Hayashi, & others) 1991;51:110–12,CR

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- Spinal cord protection during aortic occlusion efficacy of intrathecal tetracaine (Breckwoldt, Genco, & others) 1991;51:959–63*

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- Current surgical technique to repair Fallot's tetralogy with absent pulmonary valve syndrome (Snir, de Leval, & others) 1991;51:979–82*

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- Strut fixation of an extensive flail chest (Landreneau, Hinson, & others) 1991;51:473–5,CR
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- Should we care? Do we care? What should we do? (Peters) 1991;51:807–8,ED
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Herbert Sloan, MD

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1992 Annual Meeting of The Society of Thoracic Surgeons

The Twenty-eighth Annual Meeting will be held at The Walt Disney World Hotel in Orlando, Florida, February 3–5, 1992.

APPLICATION FOR MEMBERSHIP

(Deadline: September 1, 1992)

Requests for application forms for membership in The Society of Thoracic Surgeons should be addressed to James L. Cox, MD, Chairman, Membership Committee, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611.

The completed application forms and supporting letters must be in the hands of the Membership Committee by **September 1, 1991,** for the applicant to be considered for election at the meeting in February 1992.

CALL FOR ABSTRACTS

(Deadline: September 9, 1991)

Abstracts for papers to be presented at the 1992 Annual Meeting are now being accepted. The deadline for receipt of abstracts is September 9, 1991. No papers *received* after this date will be accepted for inclusion in this year's program. An original and one copy should be submitted, using the official Society abstract form (on verso of this page), to Delos M. Cosgrove III, MD, and Douglas J. Mathisen, MD, Co-Chairmen, Program Committee (Abstracts), The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611. Additional forms are available upon request from The Society. Abstracts must summarize an original contribution not presented or accepted for presentation elsewhere. Abstracts must be in the hands of the Program Committee by **September 9, 1991.** Abstracts received after the deadline will not be considered. It is requested that the covering letter indicate the author who is to receive notice of acceptance or rejection and the author who will present the paper.

The Thoracic Surgery Directors Association (TSDA) has established a Resident Presentation Award. Potential TSDA Resident Award abstracts must represent original work by the resident, who is to be first author and presenter. TSDA Resident Award abstracts may be directed to the regular Scientific Session or the Research Forum.

Essayists are reminded that according to the bylaws of The Society, all papers accepted for presentation: (1) must be submitted in *triplicate* to the Secretary at the time of presentation or to the Editor of *The Annals of Thoracic Surgery* prior to presentation; and (2) become the property of The Society if they are accepted for presentation.

It is well recognized that abstracts frequently belie their content by virtue of poor organization, and as a result valuable contributions to the Scientific Sessions may be unrecognized. It is important that methods and results be clearly defined in the abstract; therefore, general statements such as "results will be presented" are not acceptable. When a procedure or method is stated to have "advantages," those advantages should be defined. Abstracts that simply summarize results without defining objectives and methods are equally undesirable.

Speakers for accepted papers are limited to ten minutes.

Instructions for Abstracts

The official abstract form printed on verso of this page and available from The Society, or photocopies thereof, must be used. **Authors must categorize the principal subject of their abstract by checking the appropriate box.**

If the author wishes to submit the abstract for consideration for the Thoracic Surgery Directors Association Award competition, the *additional* appropriate box must be checked. Also, the name of the Program Director must appear on a TSDA Resident Award abstract.

1. Full names of authors must appear on the abstract.
2. Institution or address is to be given, but omit titles, degrees, and appointments.
3. Abstracts must be limited to 250 words and must be typed double-spaced.
4. When percentages are used, the absolute numbers of derivation must be stated.
5. The body of the abstract should include:
   a. A brief statement of the purpose of the study being presented, with reference to the current state of research in the field.
   b. The methods of study or experimental approach clearly, but briefly, defined.
   c. A summary of the results and/or conclusions of the study, including sufficient details to support those conclusions.
   d. A statement concerning the significance of the work and its possible implications for further research.
6. The form must be signed by the senior author attesting that the material will not be presented elsewhere if accepted for the scientific program nor published elsewhere if accepted for publication in *The Annals of Thoracic Surgery.*

In discussion of papers, The Society encourages a healthy spirit of constructive critical review and rebuttal by comments pertinent to the content of the paper being presented. Presentation of discussion in the form of "secondary papers" will not be welcomed.

CALL FOR SURGICAL FILMS OR VIDEO TAPES

(Deadline: August 27, 1991)

The popular Surgical Motion Picture program will again be presented at the Orlando meeting. The Program Committee hereby solicits the submission of surgical audiovisual presentations, which may portray a surgical procedure or simply a technical maneuver that the surgeon thinks will be of interest to The Society. The film (tape) may not exceed ten minutes in length. Sound is acceptable but not necessary; however, live narration by the principal surgeon is a requirement for participation in the movie night program. Presentations should be on 16-mm film, ¾-inch U-Matic video tape, or ½-inch VHS tape. The deadline for submission is **August 27, 1991.** Films and video tapes also should be sent to Delos M. Cosgrove III, MD, and Douglas J. Mathisen MD, Co-Chairmen, Program Committee, at The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611.

Richard P. Anderson, MD
Secretary

For Committee use only:

THE SOCIETY OF THORACIC SURGEONS

Abstract Form

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- ☐ **Great vessels**
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- ☐ **Endoscopy**
- ☐ **Vascular surgery**
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I acknowledge that the material will not be presented elsewhere if accepted for presentation on The Society of Thoracic Surgeons Scientific Program. I further understand that the Editorial Board of *The Annals of Thoracic Surgery* has the right of first refusal for publication of this material.

____
Signature of Senior Author

Information About Membership in The Society of Thoracic Surgeons

The Society of Thoracic Surgeons (STS) is the largest organization devoted primarily to the practice of thoracic and cardiovascular surgery. The major purpose of The Society is educational, with the aim of providing thoracic and cardiovascular surgeons from both academic and private practice environments a forum for presentation and discussion of scientific topics. As outlined in the original bylaws of The Society, this educational emphasis is designed to accomplish the broader goal of improving the quality and practice of thoracic and cardiovascular surgery as a specialty.

The STS recently held its 27th Annual Meeting. Since its founding in 1964, The Society has grown continually; the membership now includes the majority of board certified thoracic surgeons in the United States as well as thoracic and cardiovascular surgeons from 45 other countries.

In addition to holding an annual scientific meeting, the STS has more than 20 committees working on diverse matters related to improving thoracic and cardiovascular surgery as a specialty. Examples of these committees are: Standards and Ethics, Government Relations, Medico-Legal Affairs, Surgical Standby for PTCA, Nomenclature and Coding, Education and Resources, and Cardiothoracic Surgical Practice Guidelines. The Committee to Analyze Circulatory Assist Devices and Artificial Hearts sponsors topical meetings (next meeting, November 15–17, 1991, in San Francisco). The Committee to Develop a National Database for Thoracic Surgery has implemented the first comprehensive database program for thoracic and cardiovascular surgeons in the United States; it is currently being offered to Society members.

There are five types of membership in The Society of Thoracic Surgeons: active, senior, honorary, international, and candidate.

Active Member Applicants for active membership must be surgeons whose practice is devoted primarily to the field of thoracic and cardiovascular surgery.

QUALIFICATIONS: Applicants must be Diplomates of the American Board of Thoracic Surgery or Fellows in The Royal College of Surgeons of Canada, and be established in the practice of thoracic and/or cardiovascular surgery for a minimum of 3 years. There must be sponsoring letters from three active STS members.

Senior Member Any active member or international member, upon reaching the age of 65 years, shall automatically become a Senior Member.

Honorary Member Honorary membership shall be reserved for distinguished persons worldwide who have achieved prominence in the field of thoracic and cardiovascular surgery and have contributed to its advancement. Honorary members shall be elected by a majority vote of The Society at its annual business session upon recommendation of the Council of the STS.

International Member Members from countries other than the United States and Canada were previously accepted only as active members. Because of differences in training and practice, the application process for foreign members was often complex and time consuming. To allow for greater international participation, the bylaws were revised to provide for the category of international member.

QUALIFICATIONS: Applicants shall reside outside the United States and Canada. They shall have completed training equivalent to that required for active membership. They shall have achieved appropriate certification or recognition of achievement in the specialty in their country and must devote the majority of their professional efforts to the interests of the specialty. Appropriate documentation of professional achievements shall be provided to the Membership Committee.

Candidate Member The candidate membership category was created to allow participation of younger surgeons not yet qualified for active membership.

QUALIFICATIONS: Applicants shall be enrolled in a thoracic and cardiovascular training program accredited by the Residency Review Committee for Thoracic Surgery under the authority of the Accreditation Council for Graduate Medical Education or in a training program similarly approved by The Royal College of Surgeons of Canada. Also, individuals who have completed their training in one of the above programs and are in process of acquiring certification or have been certified by the American Board of Thoracic Surgery or The Royal College of Surgeons of Canada and are awaiting fulfillment of the 3-year residence requirement for active membership are eligible for this type of membership.

If you would like to receive an application for membership in The Society, send the request printed below. This year's deadline for receipt of applications is September 1, 1991. We suggest you apply soon as it takes time to process the application. Approved applications will be presented to the membership at the February 1992 Annual Meeting in Orlando, FL.

REQUEST FOR APPLICATIONS

Please send an application for: ☐ Active membership ☐ International membership ☐ Candidate membership

TO: NAME: ____________________

ADDRESS: ____________________

____

TELEPHONE NUMBER: ____________________

Send to: James L. Cox, MD, Chairman, Membership Committee
The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611
Telephone: (312) 644-6610; FAX: (312) 527-6635

THE
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*Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association*

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

Warm Heart Surgery: Theory, Concepts and Practice, Toronto, Ontario, Canada—June 20, 1991

For information on this meeting, contact Continuing Education, Faculty of Medicine, University of Toronto, Medical Sciences Building, Toronto, Ont M58 1A8, Canada; or telephone (416) 978-2718.

Seventeenth Annual Meeting of The Western Thoracic Surgical Association, Seattle, Washington—June 26–29, 1991

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Second International Seminar on Transplantation for End-Stage Lung Disease, Zurich, Switzerland—June 27–28, 1991

For information on this meeting, contact A.K.M. Congress Service, Clarastrasse 57, Ch 4005 Basel, Switzerland; or telephone 061-691-8888 (facsimile: 061-691-8189).

Techniques in Pulmonary and Oesophageal Surgery, Liverpool, England—July 14–16, 1991

For information on this meeting, contact Mr R. J. Donnelly, The Cardiothoracic Centre, Broadgreen Hospital, Thomas Dr, Liverpool L14 3LB, England; or telephone 051 228 4878 (facsimile: 051 220 8573).

Twentieth World Congress of The International Society for Cardiovascular Surgery, Amsterdam, the Netherlands—September 1–6, 1991

For information on this meeting, contact the Registrar: XX World Congress—ISCVS, International Travel Service, Inc, 104 Wilmot Rd, Suite 300, PO Box 825, Deerfield, IL 60015; or telephone (708) 940-2100 (facsimile: (708) 940-2386); or contact the Congress Secretariat, International Society for Cardiovascular Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

Current Issues in Thoracic Organ Transplantation, Essen, Germany—September 19–21, 1991

For information on this meeting, contact Organizing Secretariat, Gisa Brodde Meetings, Saalbau Essen, PO Box 100301, D-4300 Essen 1, Germany; or telephone (0)201-232121 (facsimile: (0)201-232273).

Heart Valve Replacement—Past Performance: Future Prospects, Sheffield, United Kingdom—September 19–21, 1991

For information on this meeting, contact Jenny Pupius, Symposium Secretariat, Department of Medical Physics and Clinical Engineering, Royal Hallamshire Hospital, Glossop Rd, Sheffield S10 2JF, United Kingdom; or telephone (0742) 555250 (facsimile: (0742) 729981).

Fifth Annual Meeting, European Association for Cardio-Thoracic Surgery, London, United Kingdom—September 22–25, 1991

For information on this meeting, contact Organising Secretariat, Conference Associates & Services, Ltd, Congress House, 55 New Cavendish St, London W1M 7RE United Kingdom; or telephone 071 486 0531 (facsimile: 071 935 7559; telex: 934 346 CONFAS G).

Fifth Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery, Alexandria, Egypt—September 23–27, 1991

For information on this meeting, contact Prof M. El-Fiky, Chairman, Cardiac Surgery Department, Ain Shams Faculty of Medicine, Abbassia, Cairo, Egypt; or telephone (202) 834981 or (202) 835495 (facsimile: (202) 834981).

Arterial Grafts for Coronary Bypass Surgery, Brussels, Belgium—September 29–October 2, 1991

For information on this workshop, contact R. Dion, MD, Cliniques Universitaires St. Luc, Chirurgie Cardiaque, ave Hippocrate, 10, B 1200 Brussels, Belgium; or telephone 32/2/764.61.06 or 764.61.07 (facsimile: 32/2/764.37.03).

Mitral Surgery Advances and Controversies, Varese, Italy—October 4–5, 1991

For information on this meeting, contact Erreci Congressi sri, Via Negroni, 4/7, 28100 Novara, Italy; or telephone 0321-393021 or 398977 (facsimile: 0321-393026).

American College of Surgeons, Chicago, Illinois—October 20–25, 1991

For information on this meeting, contact American College of Surgeons, 55 Erie St, Chicago, IL 60611; or telephone (312) 664-4050.

Fifty-seventh Annual Scientific Assembly, American College of Chest Physicians, San Francisco, California—November 4–8, 1991

For information on this meeting, contact the American College of Chest Physicians, 911 Busse Highway, Park Ridge, IL 60068; or telephone (708) 698-2200.

Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, Florida—November 7–9, 1991

For information on this meeting, contact Hendrick B. Barner, MD, Southern Thoracic Surgical Association, 401 N Michigan Ave, Chicago, IL 60611-4267; or telephone (312) 644-6610 (facsimile: (312) 321-6869).

Third Combined Meeting of the Nederlandse Vereniging Voor Thoraxchirurgie and the Deutsche Gesellschaft für Thorax-, Herz- und Gefäßchirurgie, Maastricht, the Netherlands—November 7–9, 1991

For information on this meeting, contact Organizing Secretariat, Conference Agency Limburg, Mrs Brigitte Bessems, c/o University Hospital Maastricht, PO Box 1918, 6201 BX Maastricht, the Netherlands; or telephone 31 (0)43 258344 (facsimile: 31 (0)43 258355).

Sixth World Conference on Lung Cancer, Melbourne, Australia—November 10–14, 1991

For information on this meeting, contact Ms Jane Willis, MCS Convention Services, PO Box 335, Heidelberg, Vic 3079, Australia; or telephone (613) 499-6722 (facsimile: (613) 499-7137).

Sixty-fourth Scientific Session of the American Heart Association, Anaheim, California—November 11–14, 1991

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 750-5300.

Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, Florida—February 3–5, 1992

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

Forty-first Annual Meeting of the American College of Cardiology, Dallas, Texas—April 12–16, 1992

For information on this meeting, contact American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814; or telephone (800) 253-4636.

Seventy-second Annual Meeting of the American Association for Thoracic Surgery, Los Angeles, California—April 27–29, 1992

For information on this meeting, contact American Association for Thoracic Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

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SITUATIONS AVAILABLE

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 398. 398C/I

Thoracic/vascular surgeon needed to join prominent, active 3-man group in desirable suburban community in greater NY metropolitan area. Excellent opportunity for well-trained, highly motivated individual. Recent graduate preferred. Possible academic affiliation. Please respond with CV.

Please respond to Box 404. 404D/I

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in Dallas. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Respond to Practice Enhancement Resources, PO Box 655999, Dallas, TX 75265; Attention: Carol. 487B/F

Cardiovascular and thoracic surgeon to join established 3-man private practice in mid-South. Practice includes thoracic, cardiac, and vascular surgery. Must be board certified or eligible in thoracic and cardiovascular surgery. Prefer candidate who has recently completed his/her training. Please respond with curriculum vitae.

Please respond to Box 489. 489B/G

Cardiovascular/thoracic surgeon wanted to join principal in metropolitan city on west coast of Florida. Must be ABTS certified or eligible and hold Florida license. Good opportunity for young, aggressive, energetic individual. Experience in cardiac transplantation an asset.

Please respond to Box 491. 491B,D,F

Cardiothoracic surgeon to join group of two, in Michigan. Please respond with CV and references.

Please respond to Box 504. 504C/H

Cardiovascular surgeon to join a young diplomate, ABTS, in a practice that has grown to some 600 hospital surgeries per year. Location is in a city in the mid-South. The only open heart program in 15 counties. 325-bed regional medical center, 2 catherization labs. Practice consists of cardiac, thoracic, and vascular surgery. Full financial support including productivity incentive. All benefits, malpractice and office expenses provided.

Please respond to Box 511. 511C/F

Cardiovascular and thoracic surgeon, BC/BE, recently trained, to join an established 3-man private practice group in Southeastern coastal capital city and two-university town. Great hunting, fishing, and sports. Submit CV and references.

Please respond to Box 519. 519D/I

Cardiac surgeon, ABTS eligible/certified. Position available immediately to join established 4-surgeon group practicing adult cardiac surgery. Excellent opportunity for new or recent grad. Practice located in Reading, PA (southeast PA within easy distance of New York and Philadelphia). Guaranteed starting salary and excellent benefits.

Send CV and references to Ashworth and Gregory MDs, 1235 Penn Ave, Wyomissing, PA 19610; (215) 374-5000. 520D/F

Pediatric cardiac surgeon to assume responsibility for established (120 cases per year) and growing pediatric cardiac program as of July 1, 1991.

Address correspondence to Neil R. Thomford, MD, Professor and Chairman, Department of Surgery, Medical College of Ohio, PO Box 10008, Toledo, OH 43699-0008. 522D/G

Assistant surgeon sought for busy adult cardiothoracic surgery practice. Entire responsibility will be to assist four senior surgeons in the operating room. Board certification or eligibility in general surgery, and some experience in vascular and/or thoracic surgery, desirable. Must be licensed in Pennsylvania or able to obtain license. Generous salary and fringes. Position is available immediately and could be permanent. Ideal location in very pleasant, small city near major eastern metropolitan centers.

Please respond with CV to Lawrence I. Bonchek, MD, 555 N Duke St, Lancaster, PA 17603; (717) 295-8395. 527E/F

Cardiothoracic surgeon—board certified/eligible and recently trained, to join an established and expanding private practice of cardiac surgery.

Please respond with curriculum vitae and details of experience to John M Postel, MD, Chief of Cardiac Surgery, Cedars Medical Center, 1400 NW 12th Ave, Miami, FL 33136. 528E/G

Cardiothoracic/vascular surgeon, BE/BC, wanted to join growing practice in New Jersey. Recent graduate preferred. Please respond with CV.

Please respond to Box 529. 529E/G

Director, cardiac transplant program—The Department of Surgery, Medical College of Ohio, is seeking a board certified or board eligible cardiothoracic surgeon to direct established heart transplant program.

Curriculum vitae and bibliography should be submitted to Neil R. Thomford, MD, Chairman, Department of Surgery, PO Box 10008, Toledo, OH 43699-0008. The Medical College of Ohio is an equal opportunity employer. 530E/G

Thoracic surgeon wanted: a busy general thoracic surgical practice (non–open-heart, nonvascular) 20 miles south of Boston seeks to add a third surgeon. Candidate must be board certified or eligible. This active practice operates from a multihospital referral base. The community is an ideal area for family living, with excellent schools and nearby Boston and Cape Cod cultural and recreational facilities. Competitive salary, malpractice insurance, and excellent benefits package. Please respond with CV.

Please respond to Box 531. 531E/J

Thoracic/vascular surgery practice available. Established practice including noninvasive vascular lab in metropolitan Washington, DC. Physician planning to retire after 35 years. Will stay on to assure smooth transition and continuity of practice referrals.

Interested parties should send CV and letter of intent to Richard F. Cioffi, MD, Vice President, Medical Affairs, Holy Cross Hospital, 1500 Forest Glen Rd, Silver Spring, MD 20910. 532E/F

Cardiothoracic surgeon needed for rapidly expanding program located in a coastal area of the Southeast. Private practice, primarily adult cardiac and thoracic. BC/BE required. Respond with curriculum vitae and names of references.

Please respond to Box 533. 533E/J

Associate director for heart transplantation is urgently needed for rapidly expanding heart transplantation program in California. Excellent benefits package. Please respond with curriculum vitae and outline of surgical experience.

Please respond to Box 534. 534E/J

Cardiovascular and thoracic surgeon: excellent opportunity for a board certified/eligible cardiovascular and thoracic surgeon to join a large cardiac surgery group in southern California. Must have a minimum of 1 year experience in pediatric and neonate cardiac surgery (including fellowship). Excellent fringe benefits. Please reply with curriculum vitae and outline of surgical experience.

Please respond to Box 535. 535E/J

Cardiothoracic surgeon needed for established cardiac program in the Philadelphia area. Must be BE/BC. New or recent graduate preferred. Salary leading to partnership.

Please send CV to Ms Rosemary Morrone, Administrator, Department of Surgery, 3 Cooper Plaza, Suite 411, Camden, NJ 08103. 536E/F

Thoracic and vascular surgeon, board certified, to join active (noncardiac) thoracic and vascular practice in northern New Jersey. Competitive salary and benefits. Please respond with curriculum vitae.

Please respond to Box 537. 537E/G

Thoracic-vascular surgeon: excellent opportunity for well-trained board certified surgeon to join and eventually buy well-established solo practice with university-affiliated hospital in large eastern city. Please submit CV.

Please respond to Box 539. 539E/G

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For details, send name and address to Dr Monroe, 7035 Hwy 6 South, Suite T 175, Houston, TX 77083. 540F

Cardiovascular and thoracic surgeon experienced in adult and pediatric cardiac surgery as well as general thoracic surgery needed to join the practice of an established cardiovascular and thoracic surgeon. Send curriculum vitae and details of experience.

Please respond to Box 541. 541F/K

Cardiothoracic and vascular surgeon, board eligible or certified, to join 2-man private practice in Ft. Lauderdale, Florida. Send CV.

Please respond to Box 542. 542F/K

Faculty position as assistant professor of cardiothoracic surgery. Candidate must be fully trained cardiac surgeon with superior abilities, committed to academic career, and willing to devote substantial time to laboratory research in area of left ventricular mechanics. Prior research experience with demonstrated productivity required. Bioengineering degree desirable. Send curriculum vitae, bibliography, and three recommendation letters. University of Pennsylvania is an equal opportunity/affirmative action employer.

Please respond to Box 544. 544F

Cardiothoracic surgeon, BC/BE, to join rapidly expanding single-hospital practice in Chicago area. Practice is 90% adult cardiac, 10% vascular with potential for general thoracic procedures. Generous salary leading to partnership. Send curriculum vitae.

Please respond to Box 545. 545F/K

Cardiothoracic/vascular surgeon: board certified in general and thoracic surgery. Minimum of 2 years of practice experience. Very active private multispecialty practice. Located in western Pennsylvania. Salary leading to full partnership. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to Box 546. 546F/K

Assistant Professor of Surgery, Cardiothoracic Surgery. This is a 3-year appointment with emphasis in general thoracic surgery, adult cardiac surgery, and experimental laboratory. Applicants must be board eligible or certified in thoracic surgery.

Submit complete curriculum vitae to John C. Baldwin, MD, Professor and Chief, Cardiothoracic Surgery, Yale University School of Medicine, 333 Cedar St, PO Box 3333, New Haven, CT 06510. Yale University is an affirmative action/equal opportunity employer. Deadline for receipt of applications is July 1, 1991. 547F

Thoracic and cardiovascular surgeon urgently needed for position with busy 2-man professional association at a large southwest medical center. Must be experienced in adult cardiac, pulmonary, esophageal, and vascular surgery. Must be board certified or eligible. Many benefits. Reply with curriculum vitae.

Please respond to Box 548. 548F/H

The Veterans Affairs Medical Center, Jackson, Mississippi, is recruiting a board certified thoracic or general surgeon to serve as Chief, Surgical Service. The incumbent will be responsible for participating in the activities of 26 surgical residents and 17 full/part-time staff physicians. The Jackson VA Medical Center is a 455-bed acute care medical center with a 120-bed nursing home care unit. There are 126 surgical beds, including a 12-bed surgical intensive care unit. Activation of a new seven-room operating suite, including ambulatory surgery, is scheduled for April 1991. The Jackson VA Medical Center is directly adjacent to the University of Mississippi Medical Center and is an integral part of its teaching programs. Applicants are expected to play a major role in these programs and must be eligible for faculty appointment.

Interested applicants should send curriculum vitae to Roland B. Robertson, MD, Chief of Staff, VA Medical Center, 1500 E Woodrow Wilson Dr, Jackson, MS 39216-5199. The deadline for application is July 1, 1991. 550F

Small Southeastern cardiology group seeking US graduate cardiothoracic surgeon with peripheral skills. Our group catheterizes 1,500 cases per year and refers 150 pump cases. Surgical coverage available.

Please respond to Box 551. 551F/G

SITUATIONS WANTED

General thoracic surgeon, 36, Canadian fellowship including training in UK. Special interest in esophageal including motility and 24-hour pH. Four years in private practice. Interested in group, academic, and/or private practice. CV and references upon request.

Please respond to Box 521. 521D/F

FELLOWSHIPS

Fellowship in cardiovascular surgery for 1 year available January 1 or July 1 with group doing approximately 1,000 cardiac procedures per year and large volume of vascular procedures. ABS eligible or certified, California medical license required or readily obtainable. Ideal for a person between general surgery residency and thoracic surgery residency.

Please respond with curriculum vitae to Bradley J. Harlan, MD, 5301 F Street, Suite 312, Sacramento, CA 95819. 480A/L

Fellowship in cardiovascular surgery available July 1, 1991. High-volume program with outstanding Fellow involvement and training. Excellent salary and benefits. American Board of Surgery eligibility required.

Please contact M. Terry McEnany, MD, Kaiser Foundation Hospital, 2350 Geary Blvd, San Francisco, CA 94115; (415) 929-5499. 513C/H

Fellowship in thoracic and cardiovascular surgery available July 1, 1991. Good salary. Research opportunities.

Please send inquiries to George C. Morris, Jr, MD, and Gerald M. Lawrie, MD, Baylor College of Medicine, Houston, TX 77030; (713) 797-9428. 538E/G

Fellowship in cardiac surgery available at the University of Massachusetts. Abundant adult cardiac experience, ideal as interim position between general and thoracic residency programs or awaiting job opportunity. Competitive salary with full benefits, Mass licensure desirable. University of Massachusetts is an equal opportunity employer.

CV and inquiries to John M. Moran, MD, 55 Lake St N, Worcester, MA 01655. 543F

Cardiothoracic surgery fellowship available July 1, 1991. Busy adult cardiac and pulmonary surgical program. Private hospital. Pleasant working conditions. Salary and benefits commensurate with experience.

Send resume to A. Hellman, MD, Open Heart Institute, 301 South Eighth St, 2-G, Philadelphia, PA 19106. 549F

Cardiac surgical fellowship: The Cardiothoracic Surgery Section at The Dartmouth-Hitchcock Medical Center is currently seeking a fellow in adult cardiothoracic surgery. The appointment will be for 1 year and available to persons PGY5 and above. The fellow will be involved in the clinical activities of a busy adult open heart and general thoracic program. Clinical research will be encouraged and supported.

Please respond with CV to William C. Nugent, MD, Chairman, Department of Cardiothoracic Surgery, Dartmouth-Hitchcock Medical Center, 2 Maynard St, Hanover, NH 03756. 551F

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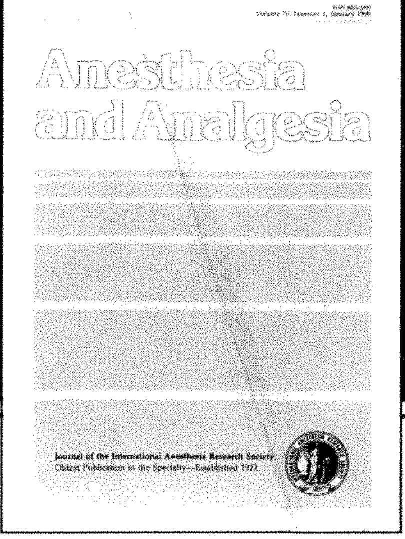

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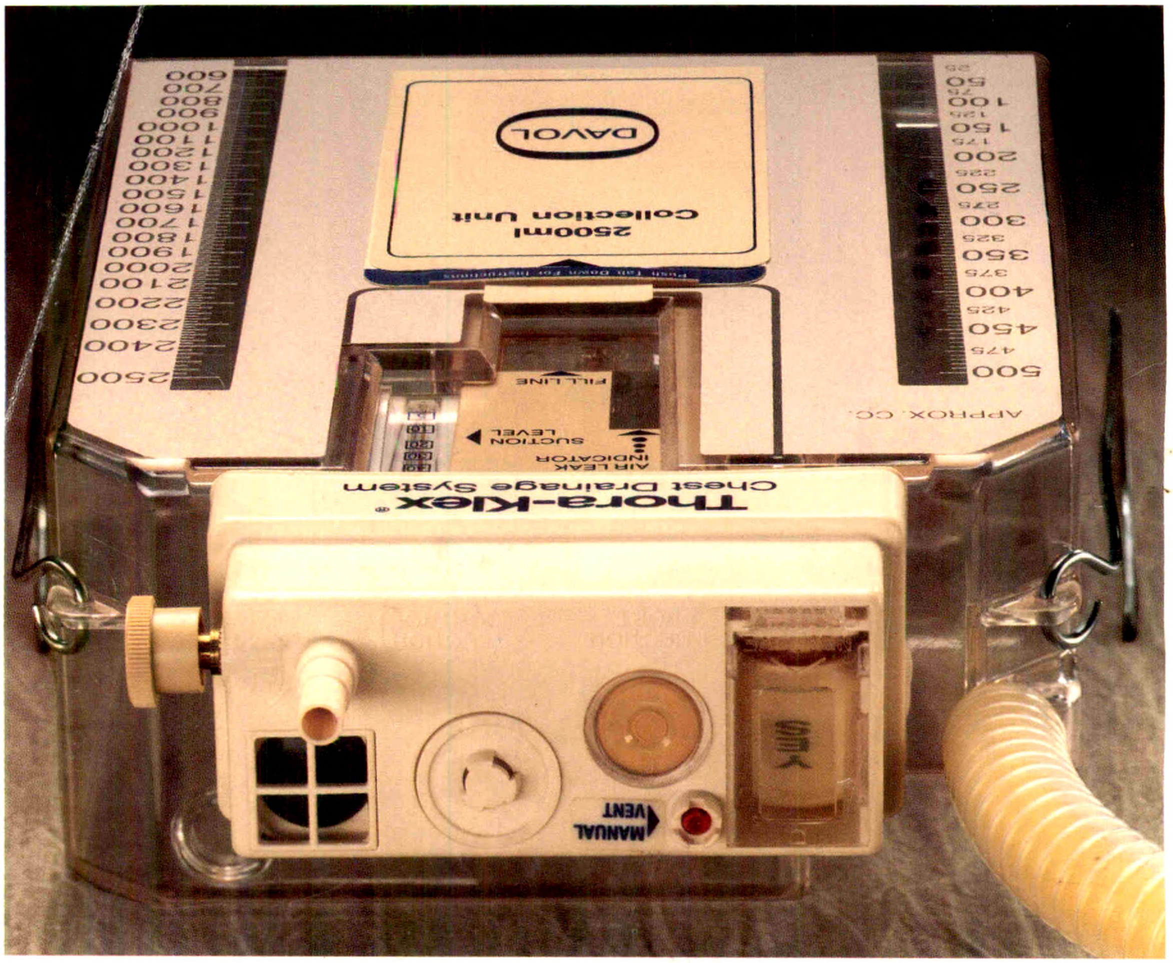

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